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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

MINISTRY OF HEALTH. **Report of the Ministry of Health for the Year 1958. Part II. On the State of the Public Health being the Annual Report of the Chief Medical Officer** [CHARLES, J. A.]. Cmnd. 871. pp. vi + 264, 1 diagram & 3 figs. London: H.M. Stationery Office. [12s.]

This admirable report follows almost exactly the pattern of previous years but in total it has 28 fewer pages and costs one shilling less than that for 1957 [this *Bulletin*, 1959, v. 34, 717]. New chapters introduced last year on young handicapped children and on accidents in the home have disappeared as well as one on the aged with mental illness: newcomers are a chapter on medical rehabilitation and a special section on the common respiratory diseases.

It is a centenary volume, as the first report *On the State of the Public Health in England* by the Medical Officer of the Privy Council appeared in 1858.

The introduction is by Sir John Charles, who again picks out with his usual skill and wisdom the salient features. The various chapters are contributed by the departmental heads under the general editorship of Dr. BALFOUR KIRK.

The population was 45,109,000: based on the vital statistics for 1958 the expectation of life at birth is 68 years for males and 74 for females: the birth rate, 16·4, was the highest for 10 years: the stillbirth rate, 21·5 per 1,000 total births, was the lowest ever recorded for England and Wales, as were the rate of infant mortality, 22·5, and the neonatal mortality, 16·2—both per 1,000 live births: the maternal mortality, 35 per 100,000 total births, and 43 including those following abortion, are, also, the lowest ever: the crude death rate, 11·7 compares with 11·5 in 1957. Heart and vascular diseases account for over half the total deaths and cancer for about a sixth: deaths from tuberculosis at 99 per million population reached a new low level.

There was a small outbreak on Merseyside of smallpox which showed unusual features: Sonne dysentery is increasing in incidence and the warning is given that to regard it "as a mild disease of low fatality ratio" is wrong: there are 280 persons with leprosy known to the department: during the year 8 deaths were due to diphtheria, 27 to whooping cough and 129 to poliomyelitis: 10 million inoculations of vaccine against poliomyelitis were given.

"It is somewhat paradoxical that we know least about those diseases which are commonest in this country" such as the common cold, chronic bronchitis and the rheumatic disorders.

Deaths from all forms of cancer numbered 95,804 which exceeds the number for 1957 by 1,787: 19,820 were from cancer of the lung and there were 2,386 from the leukaemias which is an increase of 4½ times in 30 years.

There is a note of caution lest we build extravagant hopes about the substitution of home for institutional care for the mentally disturbed. "As human society becomes more complex so will its demands upon conformity of conduct become more exacting because large defections might throw the system out of gear": this was written about problem families but it applies equally to the mentally disordered.

Fluoridation of water in the dosage recommended carries "no known risk to health".

There is an illuminating chapter on rehabilitation in which graphic details are given of the numerous people involved in the rehabilitation of a single patient who was severely paralysed: in the miners' rehabilitation service 96·7% of the patients treated were able to return to the mining industry.

A summary is given of the morbidity among 380,000 patients on the lists of 171 doctors in general practice.

There are new short sections on rabies and leprosy; there has been no human case of rabies infected in

Britain since 1911 and all the notified cases of leprosy had been infected outside Britain.

The total incidence of early infectious syphilis in patients attending the clinics for the first time is decreasing despite localized increases in certain areas, especially ports, but the steep rise in new cases of gonorrhoea continues.

There is a scholarly chapter on the common respiratory diseases and an impressive one on the work of the Public Health Laboratory Service which includes sections on tetanus spores in dressings, formaldehyde fumigation, bacterial rat poisons, Q fever, poliomyelitis virus in normal children and actinomycosis.

In the chapter on mental health it is recorded that already 29,000 defectives detained under order in institutions have been decertified and are free to leave though, in fact, few have actually gone.

There is something of interest to all public health workers in whatever branch: other matters touched on include, toxaemia of pregnancy, perinatal mortality, an outbreak of diphtheria, fluoridation of public water supplies, *Salm. typhi-murium* in abattoirs and the present state of anti-tuberculosis work.

Mention has been possible here of only a few of the features of this well written and wide-ranging report which should be studied by all concerned in the health services, curative or preventive, of the country.

It is a pity that there is no index as different aspects of the same topic are to be found, not infrequently and without cross-reference, in several sections of the report. *Allen Daley*

RAJASTHAN. MEDICAL & HEALTH SERVICES [SHARMA, B. N., Director]. **Health Statistics 1958.** pp. xiv + 48, 24 illustrations. 1959. Jaipur: Rajasthan, India.

The health statistics for this Indian State cover the period 1954–58. The population of 15,971,000 is tabulated according to sex, age and district. Only 13% of the people live in communities larger than 10,000 while 30·7% are in groups smaller than 500. Urban populations, however, grew more rapidly than natural increase would cause, indicating a drift to towns. The registered birth rate varied over the period between 13 and 14 per 1,000, and the death rate from 7 to 8·5, but the theoretically calculated rates, based on the census data of 1941–51, were 42·5 and 27·2 per 1,000 respectively. The principal causes of death were fever, followed by respiratory diseases and dysentery and diarrhoeal diseases. Smallpox was responsible for 4·4% of deaths. Mortality under 4 years of age formed almost 50% of the total deaths registered.

Cholera and plague were unimportant during the period and the main health activities were against smallpox, malaria and tuberculosis. In spite of routine vaccination smallpox incidence rose to 42·1 per 100,000 over the period, possibly owing to better reporting. About 250,000 negative reactors to tuberculin were vaccinated annually with BCG. Malaria morbidity has fallen as a result of a spraying campaign. Apart from malaria the case incidences of endemic diseases showed little decline over the 5 years. [The accuracy of these statistics is much in doubt; registered births in 1957 and 1958 were given as 108,236 and 125,415 respectively while vaccinations of infants under one year of age over the same period are given as 196,131 and 233,075.]

Medical facilities are being improved rapidly, hospital beds having increased nearly 50% over the 5 years. Specialist facilities for tuberculosis, mental, dental, paediatric and eye diseases, and several others are being increased but the needs are still great as judged by ratios of population to beds, *e.g.*, 35,000 per bed for tuberculous and 66,000 per bed for mental patients. There is now 1 doctor to 15,000 people and medical training at all levels is being expanded. Of the State revenue 7% is allocated to medical and health services. Expenditure on the latter is increasing more rapidly than on the former but even so total expenditure on curative medicine was almost 5 times greater than on health. *T. H. Davey*

LONIE, T. C. **Planning a Health Service in the South Pacific.** Reprinted from *New Zealand Branch J. Roy. Soc. Promotion Health.* 1958, Dec., No. 70, v. 23, No. 4, 22 pp.

In this essay, which contains much good sense, the author first discusses the growth of the public health services in Britain and the division of administrative responsibility between medical officers, health inspectors, and engineers, stressing the fact that although public works connected with water and sewage are now largely controlled by engineers, these highly qualified men cannot be expected to appreciate all the health implications of their work. He then goes on to discuss the training of health inspectors and their standing, which is high and should remain so.

In the South Pacific the public health organizations are still immature and under-staffed. The author strongly advocates the separation of the curative from the preventive services, because though many attempts have been made to combine them, they have never been successful. For medical practitioners and health inspectors the Central Medical School and the Central School of Hygiene at Suva, Fiji, have for many years been the active and successful centres of training. From them the medical practitioners go out with a good status, but this is not always true of the inspectors, who are trained to subordinate work and given a certificate of comparatively less value. The suggestion is made that the Fiji Examination Board of the Royal Society of Health should be revived, to give a qualification of more than local reputation. Status is important. *Charles Wilcocks*

BAUMGARTNER, Leona & GRAD, F. P. **A New Health Code for New York City.** *Amer. J. Pub. Health.* 1959, Oct., v. 49, No. 10, 1313–28. [32 refs.]

Dr. Baumgartner is the distinguished Health Commissioner for New York City and Mr. Grad is the Associate Director, Legislative Drafting Research Fund, Columbia University.

The Board of Health of New York City adopted a

new Health Code in March 1959. It replaces the former Sanitary Code, contains 325 pages and is the result of 3½ years of deliberation.

This article describes how and why the revision was undertaken and the main contents of the new Code.

The last previous revision of the Sanitary Code had been in 1914 and it eventually contained hundreds of amendments: it was not only complicated but seriously out-of-date. The detailed research for the new code, apart from staff time in the health department, cost about $160,000, part of which came from educational foundations.

Questions of public health policy were dealt with by the Board, or department, of Health and those of legal drafting by a team of 5 lawyers and 2 secretaries from the Legislative Drafting Research Fund.

The constitution of the Board of Health derives from the City Charter: it consists of the chairman and 4 members, 2 of whom must be medical: the chairman is *ex officio* the Commissioner of Health: all are appointed by the Mayor: the Board of Health is the "final legislative authority in matters of health affecting the city" but no enactment must be inconsistent with the constitution and laws of the State. The penalties for infringement of the code are fines not exceeding $500 or imprisonment for not exceeding one year.

The revision entailed many sessions for consultation between the sections of the health department which enforce the code and the lawyers: also with officials of State and other city departments. A draft, prepared after these meetings, was widely circulated inside and outside the department including copies to trade organizations and technical experts. All comments received were carefully considered, after which a draft was submitted to the Board of Health. The Board then met the Commissioner's staff and the legal advisors in executive session. This procedure was adopted section by section and the draft so prepared was given provisional approval by the Board of Health and then re-circulated. Finally all the sections were combined, the further comments discussed and final approval given.

The new Code is not a consolidation of previous legislation but is a completely new one: it contains notes explaining the changes made and the reasons therefor.

There are 5 sections: I deals with general matters such as powers of inspection, permits and registrations, abatements of nuisances and certain parts of food and drug law: II covers communicable diseases, clinical laboratories, blood and plasma banks, blood donations and transfusions and artificial human insemination: III is about the Maternal, Infant, Child and School Health Services and defines the qualifications of the chiefs of the obstetrical and paediatric services in hospitals; it sets out standards for day nurseries, nursery schools, children's institutions and child minders: IV concerns itself with foods, drugs and cosmetics and environmental sanitation: it also includes radiation hazards and requires the registration of all radiological installations: V covers vital statistics, registration of births and deaths, burials and cremation.

The removal of out-of-date requirements often met with resistance. The new approach to control has been one of flexibility despite the fact that this leads to greater difficulty in obtaining court convictions than if the Code were rigid and specific. But education and persuasion are regarded as more valuable than frequent resort to the courts and the imposition of small fines.

Care was taken to avoid overlapping with Federal and State laws particularly in the food and drug field. It was decided to leave economic fraud to these other legislations.

New views on epidemiology have led to the abandonment of quarantine requirements and the placarding of premises where there is a case of infectious disease: the annual examination of food handlers has been discontinued and replaced by a requirement that "no person knowingly employ a food handler who is afflicted with a communicable disease".

The revision has been a formidable task but the benefits to New Yorkers, to business interests and to the officials responsible for enforcing the Code are incalculable. The authors maintain that it is not a "model" even for other American cities but it will, undoubtedly, be of great help to all in many countries where existing codes or laws are in need of revision.

Allen Daley

MATERNAL AND CHILD HEALTH

LEVIN, B. [M.D., Ph.D.], MACKAY, Helen M. M. [M.D., F.R.C.P.], NEILL, Catherine A. [M.D., M.R.C.P.], OBERHOLZER, V. G. [B.Sc.] & WHITEHEAD, T. P. [F.R.I.C.]. **Weight Gains, Serum Protein Levels, and Health of Breast Fed and Artificially Fed Infants, Full Term and Premature. A Clinical and Biochemical Study based on 946 Infants and Children at the Mothers' Hospital (Salvation Army) and the Queen Elizabeth Hospital for Children, London.** *Med. Res. Council Spec. Rep. Ser. No. 296.* pp. ix + 154, illustrated. 1959. London: H.M. Stationery Office. [16s.]

This report is based on a study of 521 full term and 223 premature infants. The analysis shows that the growth curves of each group, compared on a basis of age from conception, are indistinguishable. There was no significant difference between the growth rates of breast-fed and artificially fed children.

The serum protein values provide standards for normal children. As for growth, the premature infants do not differ from the full term when related to conceptual age. The globulin level, which was higher at birth than it is in adults, dropped by a fifth in the first 5 weeks and remained at this lower level for the next 18 months. The whole of the fall was accounted for by the fall in the gamma globulin.

[The collection of this useful—and even interesting—material was completed in 1950. A modest paper, some

20–30 pages long, could have been published in 1951. Somehow in the course of 9 years, it has become swollen into a monograph of 154 pages, which is dull, often obscure and sometimes repetitious. It is a wise rule that the publication of results should be quick and concise.] *R. Passmore*

CHRONIC CARDIO-RESPIRATORY DISEASES

MIALL, W. E. **Follow-Up Study of Arterial Pressure in the Population of a Welsh Mining Valley.** *Brit. Med. J.* 1959, Dec. 5, 1204–10, 2 figs. [20 refs.]

During 3 months of the winter of 1953–54 arterial blood pressure measurements were made in a random sample of the general population of the Rhondda Fach valley in South Wales (*Clin. Sci.*, 1955, v. 14, 459). The sample consisted of 250 families and all first-degree relatives living within 25 miles. 4 years later during the same 3 months of the winter of 1957–58 the measurements were repeated under exactly comparable conditions in the survivors of the original population. This numbered 1,226 but meantime 66 had left the area, 41 were dead and 5 refused to assist in the follow-up. Thus repeat measurements were obtained for 1,114 (99·6%) of the 1,119 subjects still alive and resident within 25 miles of the valley.

Casual blood-pressure measurements were made, as in the original enquiry, by the same observer using the same technique. Medical, obstetrical and occupational histories were brought up-to-date and measurements were made of height, weight, girth and arm skinfold. All these new measurements were made without reference to previous records. As other observers had recently claimed that hypertension is commoner in those who customarily take additional salt with their food than those who do not, questions about salt intake were added.

The results suggest the possibility that arterial pressure, when full allowance is made for age, may be increasing in middle-aged males. This trend is occurring to a greater extent in men previously engaged in heavy jobs, though they still have lower pressures than those previously in light occupations. These findings may be significant when considered against the secular trend of mortality in middle-aged males as recorded by the Registrar General. Blood pressure was again found to correlate with family size. In women, those adding salt at table to cooked meals, who presumably have a larger salt appetite, were found to have lower blood-pressures and smaller pulse-pressures in 1958, to have gained less in blood-pressure and pulse-pressure during the previous 4 years, and to be lighter than women who do not take additional salt in this way. No comparable differences were found in men.

A. Meiklejohn

MORRIS, J. N. **Occupation and Coronary Heart Disease.** *Arch. Intern. Med.* 1959, Dec., v. 104, No. 6, 903–7.

A review of the subject.

FLICK, A. L. & PATON, R. R. **Obstructive Emphysema in Cigarette Smokers.** *Arch. Intern. Med.* 1959, Oct., v. 104, No. 4, 518–26, 6 figs. [29 refs.]

In a search for a constant definition of emphysema, the authors considered that Laennec's original observation had not been bettered; this of course is a clinical observation. They then defined obstructive emphysema by the presence of lower respiratory obstruction in a patient who has not had juvenile or adolescent asthma, who does not have pneumoconiosis, and does not have more than minimal granulomatous lung disease. This definition does seem fairly wide. They endeavoured to delineate its relationship to smoking. 222 male patients were examined in Seattle between August and November 1958. Detailed history regarding smoking habits and lower respiratory symptoms, a physical examination, and maximum expiratory flow rates (MEF) were obtained. All the patients in a male ward, with certain exceptions, were included, but in the second half of the study men under 40 years of age were not included. The amount of smoking was extimated in "pack years"; a "pack year" being the number of years of smoking × the number of cigarettes a day, divided by 20. The maximal expiratory flow rate was then estimated. The best single reading of 5 or 10 tries was recorded; in all instances there were at least 3 values agreeing within 15 litres per minute. Pipe and cigar smokers were classified as non-smokers. Tables are given showing the following results:—

Among smokers there is a distinct decline in MEF, which is seen in many to begin about 40 years of age, and progresses thereafter. Among non-smokers no apparent change is noted until 70 years. In a few patients, however, this phenomenon is not found. When the patients are classified by age there is definite reduction in the graph of the MEF among smokers as compared with non-smokers, and this increases with age. As the number of "pack years" increases so does the reduction in MEF. Among smokers the lengths of the cigarette butt ends was estimated. Those who left cigarette butt ends of 30 mm. or more had a smaller reduction of MEF than those who left butts of less than 30 mm. The authors then discuss the pathogenesis of emphysema briefly with emphasis on terminal bronchiectasis as the primary lesion. Their definition of obstructive emphysema may not be agreed by some observers. It was certainly extraordinary that there was no diminution of MEF among non-smokers up to the age of 70. *F. H. Young*

See also p. 346, KEATINGE, BUXTON & HUNT, **A Study of the Incidence of Bronchitis amongst some Foundrymen in Derbyshire and Nottinghamshire, compared with a Contrasting Occupational**

Group, and a Geographical Study of Bronchitis Mortality in the Foundry Workers of England and Wales.

MOYES, E. N. & KALINOWSKI, S. Z. **Prophylactic Chemotherapy in Chronic Bronchitis.** *Tubercle.* 1959, Apr., v. 40, No. 2, 112–18. [13 refs.]

The authors in this paper continue their trials of the prophylactic use of antibiotics previously reported (MOYES and KERSHAW, *Lancet*, 1957, v. 2, 1187). Regarding the use of long-term tetracycline as of proved value but very expensive, they tried 4 different regimes on 98 patients (5 had to drop out of the trial).

Group 1: 25 patients—erythromycin 1 gm. daily for 7 days, thereafter courses of 1 gm. daily for 5 days taken at the first signs of symptomatic deterioration.

Group 2: 25 patients—erythromycin 1 gm. daily for 7 days followed by a regular course every 4 weeks of 1 gm. daily for 5 days.

Group 3: 23 patients—tetracycline 1 gm. daily for 7 days, thereafter courses of 1 gm. daily for 5 days as in Group 1.

Group 4: 25 patients—tetracycline 1 gm. daily for 7 days followed by 750 mgm. daily for 4 months.

The patients appear to have been fairly selected and the trial was soundly conceived. Adequate bacteriology was carried out. In Group 4, 60% of the patients were materially benefited; in Group 3 benefit was obtained in 48%. In Groups 2 and 1 (erythromycin) 23% and 24% were benefited. The reduction in the amount and purulence of the sputum was a valuable guide to the likely results. Reduction of dyspnoea was difficult to assess. Diarrhoea which occurred in 30% of the patients was the only troublesome complication.

Exacerbations are best estimated by the loss of time away from work. Here, although not statistically significant, the time lost was reduced in all groups but the tetracycline groups fared best.

Bacteriologically at the end of 7 days Groups 1 and 2 lost their *Haemophilus influenzae* in 9 (39%) patients compared with 25 (86%) in Groups 3 and 4. There was little difference between the groups in their loss of *Streptococcus pneumoniae* and *Staphylococcus pyogenes.*

It is concluded that for routine work the difference between results in Groups 3 and 4 does not justify the extra expense, though the continuous regime was used in selected cases. Erythromycin has no place in the routine treatment of chronic bronchitis. [This paper is worth reading in full.] *F. H. Young*

CANCER

WYNDER, E. L., LEMON, F. R. & BROSS, I. J. **Cancer and Coronary Artery Disease among Seventh-Day Adventists.** *Cancer.* Philadelphia. 1959, Sept.–Oct., v. 12, No. 5, 1016–28, 14 figs. [14 refs.]

The religion of Seventh-Day Adventists prohibits smoking and drinking. Their actual habits in these and other respects were obtained by interviewing 463 men and 494 women and contrasting them with 417 men and 404 women of other persuasions. The vast majority of the Seventh-Day Adventists were non-smokers and non-drinkers though a substantial proportion of the converts to the faith had not always been so. Compared with the controls they had also a much lower intake of meat, fish, coffee and tea. They did not materially differ in their occupations or area of residence in Los Angeles—22% men and 19% women lived in the part with most air pollution compared with 28 and 25% of the controls. From 8 hospitals under the direction of the Seventh-Day Adventist Church, records were extracted of nearly 12,000 patients with cancer, coronary artery disease or myocardial infarction. During approximately the same period 9·4% of the total admissions from all causes were of Seventh-Day Adventists. This proportion therefore has been applied to the admissions from specific forms of cancer or heart disease to give the number of Seventh-Day Adventists "expected" among them. With malignant disease in men the most striking discrepancies lie in cancer of the lung (excluding adenocarcinomas), of which cases 2 were observed in Seventh-Day Adventists and 15 were expected, and cancer of the mouth, larynx and oesophagus, of which 2 were observed and 16 expected. All other primary sites of growth showed some reduction but none to so great or so significant an extent. Both the lung cancer cases had been previous cigarette smokers who had smoked one packet a day for at least 20 years but had given up 14 and 5 years ago respectively.

With the women there was no excess of epidermoid cancers of the lung (3 observed and 3 expected) and the only large differences lay in cancer of the cervix (12 Seventh-Day Adventists to 30 expected) and of the mouth, larynx and oesophagus (1 observed and 6 expected).

In the admissions of the general population there were 5 times as many men with cancer of the lung as women and nearly 3 times as many with cancer of the mouth, larynx and oesophagus. In the Seventh-Day Adventist group the numbers were about equal, a result which is in keeping with previous estimates that lung and upper respiratory tract cancers occur at about the same frequency in the 2 sexes in non-smoking populations. Similarly with myocardial infarction the sex ratio is about 1 : 1 in the Seventh-Day Adventists and nearly 2 M : 1 F in the non-Seventh-Day Adventists. The observed number of cases in women

Seventh-Day Adventists is not significantly different from the number expected whereas with the men Seventh-Day Adventists the observed number is only half the expected. The same trends are noted with coronary artery disease.

These data come from Los Angeles and it is concluded that while they do not rule out that its air pollution could act as a co-factor to tobacco smoke, they do indicate that the air pollution alone in the absence of tobacco smoking has had no significant influence on the development of cancer of the respiratory tract up to the present time.

The evidence on heart disease leads to the suggestion that smoking plays some part in precipitating infarction, particularly in the younger person.

It has been suggested that the association between lung cancer and smoking may be due to genetic factors —that a person inherently predisposed to lung cancer is also inherently predisposed to smoke cigarettes. With the present data one must go further and assume that the genetic or other predetermination applies not only to whether or not a person will develop lung cancer and whether or not he will smoke cigarettes but also as to whether or not he or she is brought up or converted into the Seventh-Day Adventist Church.

[This paper is an interesting preliminary to a large-scale prospective study of Seventh-Day Adventists. Its statistics need to be read with some care since they contain a number of minor errors, *e.g.* the percentages of Figures 1 and 2 do not agree with the corresponding figures given in the text; cancer of the stomach is said to be 62% lower than expected when it is 62% of the expected; for women the observed adenocarcinomas of the lung are said to be within 90% of the expected number and the reference should apparently be to epidermoid cancers; the expected numbers are said to be based upon a proportion of 9·4% but this is certainly not true of all of them.] *A. Bradford Hill*

BURNEY, L. E. **Smoking and Lung Cancer. A Statement of the Public Health Service.** *J. Amer. Med. Ass.* 1959, Nov. 28, v. 171, No. 13, 1829–37, 6 figs. [Numerous refs.]

With many references to the new extensive literature the Surgeon-General, United States Public Health Service, reviews very briefly the evidence of the close association between the occurrence of lung cancer and cigarette smoking, the objections that have been made to a direct cause-and-effect interpretation of the association and the possible rôle of air pollution as a factor of importance in its aetiology. He puts forward a possible concept of pathogenesis as follows:

> "Tars containing benzpyrene and probably other carcinogens present in cigarette smoke (or contaminated air) are absorbed by the cells of the respiratory tract, especially in the alveoli. Here these foreign particles are picked up by phagocytes and transported toward the trachea in the mucous blanket of the bronchi. En route, concentration occurs where the cilia of the bronchial mucosa are injured or absent, and the motion of the mucous blanket is stopped for appreciable lengths of time. During this period the carcinogens contained in "tar" particles and in the mucus are afforded prolonged contact with the underlying bronchial cells, which react by malignant change."

There is at present no experimental proof of this concept and the findings of animal experiments are so far inconclusive. Under possibilities for prevention the Surgeon-General is sceptical of the value of filter tips. He finally concludes:

> "It is a statutory responsibility of the Public Health Service to inform members of the medical profession and the public on all matters relating to important public health issues. The relationship between smoking and lung cancer constitutes such an issue and falls within this responsibility of the Public Health Service.
>
> "The Public Health Service believes that the following statements are justified by studies to date.
>
> 1. The weight of evidence at present implicates smoking as the principal etiological factor in the increased incidence of lung cancer. 2. Cigarette smoking particularly is associated with an increased chance of developing lung cancer. 3. Stopping cigarette smoking even after long exposure is beneficial. 4. No method of treating tobacco or filtering the smoke has been demonstrated to be effective in materially reducing or eliminating the hazard of lung cancer. 5. The nonsmoker has a lower incidence of lung cancer than the smoker in all controlled studies, whether analyzed in terms of rural areas, urban regions, industrial occupations, or sex. 6. Persons who have never smoked at all (cigarettes, cigars, or pipe) have the best chance of escaping lung cancer. 7. Unless the use of tobacco can be made safe, the individual person's risk of lung cancer can best be reduced by the elimination of smoking." *A. Bradford Hill*

KAPLAN, I. **Relationship of Noxious Gases to Carcinoma of the Lung in Railroad Workers.** *J. Amer. Med. Ass.* 1959, Dec. 12, v. 171, No. 15, 2039–43, 1 fig. [11 refs.]

Study has been made of the medical records of the Baltimore and Ohio Railroad relief departments over the 6 years 1953–58. Among 12,000 employees directly exposed to exhaust fumes from diesel or steam engines (drivers, firemen, etc.) there were 49 deaths from lung cancer and at national death rates 56 would have been expected. Among 20,000 manual workers exposed to a lesser degree (electricians, blacksmiths, carpenters, etc.) there were 67 observed deaths and 93 expected; and among 7,000 rarely or not at all exposed (mainly clerks) there were 38 observed deaths and 42 expected. The observed lung cancer deaths were therefore only 87·5, 71·6 and 89·4% of those expected at the national rates. In other words there was no evidence of an association between the exposure to noxious fumes and the lung cancer mortality.

[The comparisons are restricted to lung cancer and it would have been of value to see also the relative positions of the 3 groups for other forms of cancer and other causes of death.] *A. Bradford Hill*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Atmospheric Pollution; Port, Ship and Aviation Hygiene; Infestation.**

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

LJUTOV, V. **Technique of Indole Test.** *Acta Path. et Microb. Scandinavica.* 1959, v. 46, No. 4, 349–60, 1 fig, [22 refs.]

A study has been made of the best technique for the indole test [see also BURMAN, *Proc. Soc. Water Treatment and Examination*, 1955, v. 4, 10].

The number of positive indole results obtained depended upon the brand of peptone used. Extraction with ether increased the number of positive results but there were still differences between brands of peptone. The addition of 0·1% tryptophan to the medium eliminated the difference between peptones and the indole production was so great that no ether extraction was necessary. The following method is therefore suggested for the indole test.

Medium. Peptone 10 gm., NaCl 5 gm, tryptophan 1 gm., aq. dest. 1,000 ml. Dissolve by steaming. Filter. Adjust to *p*H 7·5 at room temperature. Distribute in 3 ml. portions into 15 × 150 mm. tubes. Autoclave for 20 minutes at 120°C.

Incubation. 24 hours at 30–37°C.

Ehrlich's reagent. Paradimethylaminobenzaldehyde 0·8gm., amyl alcohol 92 ml., conc. HCl (spec. gravity 1·19) 13·5 ml.

Add 0·5 ml. of the reagent down the wall of the tube. Read the reaction after 2–5 minutes.

E. Windle Taylor

See also p. 353, THOMAS, HOBSON & DRUCE, *Coli-aerogenes* **Bacteria in Farm Water Supplies.**

KNAPP, W. & HAMMER, L. Vergiftung von Trinkwasser durch cyanidhaltige Abwässer. [**Poisoning of Drinking Water by Sewage Containing Cyanide**] *Arch. f. Hyg. u. Bakt.* 1959, Nov., v. 143, No. 7, 501–16, 3 figs. [18 refs.]

The increasing decentralization of industry in Germany during and after World War II has led to the establishment of old and new factories in small towns and country districts. A considerable number of metal and galvanizing works are thus in areas where their cyanide containing wastes are a potential danger to the purity of the water supply. In most instances adequate precautions and treatment of the wastes has neutralized this danger. The present paper, however, contains a detailed account of the investigations and analyses which were carried out in 3 cases where fish were poisoned by high cyanide concentrations derived from industrial wastes. There is a full discussion of the causes of these occurrences, and the inadequacy of present legal control with recommendations of the action which should be taken for their prevention.

M. E. Delafield

ATMOSPHERIC POLLUTION

MINISTRY OF HOUSING AND LOCAL GOVERNMENT. **Clean Air Act, 1956. Memorandum on Industrial Provisions.** 20 pp. 1958. London: H.M. Stationery Office. [1s.]

The Clean Air Act 1956 promises to be the most effective weapon in the struggle for clean air since legislation against the evil of smoke was introduced in the reign of the first Elizabeth. Not only are its provisions mandatory but they reflect the new positive approach to clean air. Under the Public Health Act, 1936, the Local Authority had to wait until a nuisance was committed: now they have important duties of inspection and can offer a valuable advisory service to industry. Dark smoke and black smoke are more accurately defined by reference to the Ringelmann Chart, thus giving legislation recognition to accepted practice. The Dark Smoke (Permitted Periods) Regulations, 1958 is a valiant attempt to hold the balance between the claims of the public to clean air and the difficulties of industry in performing necessary work such as soot-blowing or fire cleaning. Further provisions in favour of industry are that it is a defence to a charge of emitting dark smoke to show that it was due to (a) the lighting up of a furnace from cold, (b) to some failure of a furnace or apparatus, or (c) to the use of unsuitable fuel when suitable fuel was unobtainable. There is a further defence available until 1963 for out-of-date furnaces or equipment, where the defect is in the apparatus and not in its working, *e.g.* careless stoking. After July 1963 the type or condition of the furnace will not prevent a successful prosecution. It would seem that the combined effect of the Clean Air Act and its Regulations will soon eliminate the hand-fired boiler from industry. It has never been satisfactory and it cannot hope to survive the searching scrutiny to which its smoke must now be subjected. The Government Loan Scheme, the Income Tax Investment Allowances (Fuel Economy Plant) Order 1957, and the saving in costs which result from fuel efficiency

should combine to reconcile industry to the cost of replacing old boilers.

Perhaps even more welcome than the elimination of smoke is the reduction of dust and grit. New furnaces must now be fitted with grit and dust arresting plant, to the satisfaction of the local authority. The growing use of oil and other smokeless fuels will emphasize the weaknesses of the older plants and this combined with the vigorous implementation of the Clean Air Act should see England smoke-free in this decade.

G. Graham Don

FELDSTEIN, M., COONS, J. D., JOHNSON, H. C. & YOCOM, J. E. **The Collection and Infrared Analysis of Low Molecular Weight Hydrocarbons from Combustion Effluents.** *Amer. Indust. Hyg. Ass. J.* 1959, Oct., v. 20, No. 5, 374–8, 5 figs. [13 refs.]

SALTZMAN, B. E. & GILBERT, N. **Microdetermination of Ozone in Smog Mixtures: Nitrogen Dioxide Equivalent Method.** *Amer. Indust. Hyg. Ass. J.* 1959, Oct., v. 20, No. 5, 379–86, 5 figs. [14 refs.]

HILL, W. H. & MURPHY, Marie A. **An Appraisal of an Industrial Air Contaminant by Electrochromatography.** *Amer. Indust. Hyg. Ass. J.* 1959, Oct., v. 20, No. 5, 387–91, 5 figs.

THOMAS, J. F., SANBORN, E. N., MUKAI, M. & TEBBENS, B. D. **Identification of Aldehydes in Polluted Atmospheres and Combustion Products.** *Arch. Indust. Heath.* Chicago. 1959, Nov., v. 20, No. 5, 420–28, 6 figs. [11 refs.]

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

AMERICAN INDUST. HYG. ASS. **Industrial Noise Manual.** pp. xii + 180, numerous figs. [Numerous refs.] 1958, Apr. Detroit 27: 14125 Prevost, Michigan, U.S.A. [$7.50.]

This compilation is designed to be a comprehensive work covering the various facets of the broad subject of industrial noise, including measurement, evaluation of exposure, effects on hearing and behaviour, engineering control and personal protection, and audiometric programmes. Starting with the fundamentals of sound and noise, in a chapter entitled *Physics of Sound*, the writing progresses through a total of 10 chapters concluding with *Personal Protection in Noise Control*. The intermediate chapters are *Instruments for Sound Measurement and Audiometry*, *Technique of Sound Measurement*, *Procedure of a Noise Survey*, *Calibration*, *How We Hear*, *Effects of Noise*, *Medical Aspects of Industrial Hearing Conservation*, and *Engineering Control of Noise*.

Under the heading of physics, sound and noise are defined, and the well known relation between velocity, frequency, and wave length is presented. A definitive formula for sound pressure level in decibels is given and the method for combining the sound pressure levels of two noise sources, or for combining the levels in various octave bands to get an over-all level, is explained with a helpful chart. Typical levels of particular noises are also given and a plot of octave-band levels is introduced. Sound intensity, sound power, and power level are differentiated. Factors of importance in the calculation of sound absorption in rooms and by different building materials are also explained.

The chapter on sound-measuring instruments and audiometers is, in this reviewer's opinion, somewhat weak. Sound level meters and octave band analysers are very briefly described, and only mention is made of a peak reading instrument for measurement of impact noise. The reader instead is referred to specifications of the American Standards Association and to the various manufacturers for further information. 5 types of microphones, including the commonly supplied Rochelle-salt crystal type, are described in good detail, with advantages and limitations given for each. Auxiliary equipment such as magnetic tape recorders, oscilloscopes, and calibrators are mentioned. The text on audiometers is meagre. The chapter concludes with good photographic illustrations of sound measuring instruments and audiometers, with manufacturer, approximate price, and weight listed for each, but it is unfortunate that most of the figure numbers do not correspond with those in the text.

Technique of Sound Measurement and *Procedure of a Noise Survey* are chapters indicating that the manual as a whole is the work of a varied committee. In any case, these two chapters surpass what has gone before in content and organization. Here it is emphasized that the selection of measurement positions in any survey of noise is dictated by the purpose of the survey—that the situation to evaluate potential hearing loss is different from that of evaluating or eliminating the whine of a high-speed compressor annoying residents near a plant. Proper distinctions are made between a screening survey, a more complex octave-band survey, an engineering survey (designed solely for correction of a specific noise source, usually), and specialized procedures that may require use of a tape recorder or oscilloscope. Noise types, such as

steady or impulse or repeated impulse, wide-band or narrow-band, are well described and differences noted. There is also one of the most complete discussions that this reviewer has seen of pitfalls to be avoided in noise measurement. These pertain to the influence of environmental factors on the measuring instruments which may result in false, unduly high readings. Such influence may be microphone vibration, instrument vibration affecting vacuum tubes, an intense sound field producing vibration of vacuum tubes, electrical circuit noise, wind, or a strong electromagnetic field, such as of a large motor or generator. The discussion continues with recommendations for pre-survey equipment checks, transportation precautions (the Rochelle-salt crystal microphone can be permanently damaged by the high temperature that may develop in the boot of a car), and field calibration. Data recording and corrections are also discussed.

Acoustic (rather than electrical) calibration of sound level meters is strongly recommended for the industrial hygienist, and acoustic calibrators are available from the various manufacturers. The method is simple, but here again there can be change in a calibrator, or in an oscillator supplying the calibrator with its electrical signal, as this reviewer has experienced, that is not readily detected.

The Manual continues with good discussion of the physiology of hearing and of the effects of noise on hearing. Effects of sudden intense noise (blast effect, acoustic trauma) are differentiated from those of long continuous exposure (noise-induced hearing loss) and temporary threshold shift, or auditory fatigue, is differentiated from permanent hearing loss. The mechanism of noise-induced hearing loss is well explained as far as it is known, and various damage risk criteria are discussed. These include those proposed by KRYTER and developed by BERANEK, that of the Medical Service of the Air Force (Equivalent Exposure Time), and that of the American Academy of Ophthalmology and Otolaryngology (85 db or more in either the 300–600 c.p.s. or 600–1,200 c.p.s. bands calls for a hearing conservation programme). The conclusion of the Z24-X-2 Committee of the American Standards Association, that sufficient reliable data are not yet available (1954) for noise standards, is also presented. Annoyance due to community noise, and speech interference, are touched upon.

Medical aspects, as considered in the Manual, consist essentially of a well operated audiometric testing programme. This ordinarily includes pre-employment or pre-exposure hearing tests which serve as a base line against which to compare future tests, and periodic tests at least yearly for those exposed to appreciable noise. The pure-tone audiometer for air-conduction tests, a trained technician to conduct the tests under supervision of a physician, and an adequate testing room, are main requirements. Details of the testing and recording of the results to produce the audiogram are given, as well as a list of manufacturers of sound-insulated prefabricated rooms or booths for testing hearing. Periodic tests serve to detect early noise-induced hearing loss, usually first developing at about 4,000 cycles per second, before serious loss or loss in the speech range occurs, and indicate where steps to reduce noise exposure should be taken.

Engineering control of noise, it is pointed out, is a matter of solving problems individually, and standard procedures cannot be presented that will handle all situations. The same machine, process, or noise source in two different buildings or environments may present two greatly different problems. However, engineering control measures can be categorized, and this is handled as follows: Plant Planning, Substitution, Reduction at Source, Reduction of Transmission through Air, and Miscellaneous Methods. Substitution means the use of quieter equipment, process, or material. Numerous examples of such application are given, ranging from the use of rubber or plastic wheels on hand trucks instead of steel wheels, to the use of a hydraulic press instead of a pneumatic riveting hammer. Reduction at the source requires consideration of whether the noise is produced by a vibrating surface or by high air velocity or turbulence and includes the use of vibration isolators, as well as reducing the driving force or response of the vibrating surface. Response can be lessened by means of damping materials and techniques. The dispersive type of exhaust muffler distributes the flow over a large area, with a resulting low exit velocity and noise level. Substitution and reduction at the source require ingenuity and determination for their application, and many times experimentation as well. Reduction of noise transmission through air includes the use of enclosures lined with sound-absorbent material, to prevent reverberation where workers may be exposed, perhaps intermittently. This category also includes sound conditioning, or acoustic treatment of a room to reduce noise passage (as by hanging baffles) and reverberation, and design data for many building and interior materials are given. The section on engineering control is replete with illustrations of specific examples of industrial noise control, many showing octave-band analyses of the reduction achieved, and should serve to encourage those confronted with new or similar problems in the future.

Personal protection pertains to the use of a physical device, or barrier, which is inserted in or worn over the ear to shut out noise—the plug or insert type, and the cup or muff type. Ear protection should be considered almost as a last resort in reducing noise exposure, but in many situations it is the only practical or economical answer, at least temporarily. The theoretical limit of attenuation that may be obtained with ear protectors is about 50 decibels, because bone conduction provides an alternate path to the inner ear. Practical limits of protection are much less, owing to lack of perfect fit and leakage of noise around the protector, and experimental data on this point are given graphically for both the insert and muff types. The rubber and plastic insert types have been well received, but the muff type is sometimes indicated in ear disease or in the case of ear canals difficult to fit. Thus medical examination of the ears before use of ear protectors is necessary. Contrary to popular belief, the wearing of ear protectors in high noise levels enables one to be better able to hear speech and warning signals than without such protection, and the results of two investigators on this point are given.

This *Industrial Noise Manual* is an excellent guide for the industrial hygienist concerned with noise or for a worker newly entered in the industrial noise field. In many areas this reviewer has wished that it were more complete in text, and also that the entire manual were better organized, edited, and integrated. The many illustrations, including charts, graphs, diagrams, and photographs, are well chosen and excellent in quality, but numerous typographical errors detract from what otherwise is a quite favourable over-all impression. Subject matter has been drawn from many sources, references are listed at the end of each chapter, and a glossary is included. Medicolegal aspects of compensation for hearing loss are not considered.

Jerome K. Brasch

ROSENWINKEL, N. E. & STEWART, K. C. **Hearing Loss related to Non-Steady Noise Exposures.** *Amer. Indust. Hyg. Ass. J.* 1959, Aug., v. 20, No. 4, 290–93, 1 fig.

The noise exposure of 90 workers in 7 locations in a plant, where the noise was of non-steady characteristics such that conventional octave band analyses were not possible, was assessed by means of a Stewart noise dosimeter. (This instrument integrates over a 5 second interval the logarithm of all of the noise between 300 and 5,000 cycles/second above a 60 db threshold sensed through a weighted microphone.) The workers studied were under 35, and had had up to 10 years of noise exposure. During the sampling, a total of 12 10-minute samples, each consisting of 120 5-second integrations, were obtained at each of the 7 locations over a period of one week.

The relative noise dose rate was derived from the antilogarithm of the meter reading, and the estimated cumulative noise dose assessed from this value and the number of months' exposure for all individuals within that location.

The relationship between observed hearing loss in a test group and the calculated cumulative noise dose of the individuals has been investigated statistically, with the assumption of a linear relationship between the two variables. A significant linear relationship was, in fact, found to exist at all frequencies of 2,000 c.p.s. and over, and was most intense at 4,000 c.p.s.—the frequency most susceptible to acoustic trauma. There is evidence that rate of dosage and time of exposure are probably of equal importance in explaining observed hearing losses. Owing to the wide variance of observed hearing losses about the mean, it is not possible to use the relationship to predict hearing loss in individuals.

D. E. Hickish

MINISTRY OF LABOUR & NATIONAL SERVICE. H.M. FACTORY INSPECTORATE. **Lifting and Carrying.** *Safety, Health & Welfare, n.s. No. 1.* 12 pp., 12 figs. 1958, June. 2nd impression 1958, Oct. London: H.M. Stationery Office. [1s.]

MINISTRY OF LABOUR & NATIONAL SERVICE. H.M. FACTORY INSPECTORATE. **Safety Devices for Hand and Foot Operated Presses.** *Safety, Health & Welfare, n.s. No. 3.* 33 pp., 24 figs. 1958, June. 2nd impression (with amendments) 1958, Dec. London: H.M. Stationery Office. [2s. 6d.]

MINISTRY OF LABOUR & NATIONAL SERVICE. H.M. FACTORY INSPECTORATE. **Safety in Building Operations: Roofing.** *Safety, Health & Welfare, n.s. No. 6B.* 12 pp., 5 figs. 1958, Nov. London: H.M. Stationery Office. [9d.]

OCCUPATIONAL PHYSIOLOGY

SHEPHARD, R. J. **The Timed Airway Resistance.** *J. Physiology.* 1959, Mar. 12, v. 145, No. 3, 459–72, 7 figs. [17 refs.]

If the expiratory flow is suddenly interrupted, the pressure proximal to the obstruction rises momentarily to that of the alveoli. The transairway resistance obtained in this way probably includes a component due to tissue viscous resistance but the measurement is, nevertheless, valuable. In normal persons it was found to rise when full expiration was approached and, sometimes, to be high near full inspiration. Clearly resistance should be measured somewhere in the middle third of expiration; the author achieves this by initiating interruption at a fixed time after the start of expiration.

The interruptor method lends itself to field use and a handy portable apparatus is described in this paper.

M. L. Thomson

KILLIAN, H. Über die Grenzen der Leistungsfähigkeit manueller Beatmungsmethoden. [**Limits of Effectiveness of Manual Methods of Artificial Respiration**] *Deut. med. Woch.* 1960, Jan. 8, v. 85, No. 2, 53–7, 6 figs. [23 refs.]

Many attempts have been made to compare the effectiveness of manual methods of artificial respiration, as determined by tidal volumes, on anaesthetized subjects, on curarized subjects or even on warm cadavers. The results obtained have been widely variable apart from the Silvester and Holger-Nielsen methods which are reasonably comparable. None of the authors quoted have considered testing these methods at varying depths of asphyxia and consequently, many of the results obtained experimentally may have exaggerated values.

A series of experiments are reported where the

Silvester method of artificial respiration was adopted as a standard procedure and Röntgen-tomograms were made before and after complete relaxation had been attained by narcosis and subsequent administration of succinylcholine.

The results of this study on 5 subjects showed that the greater the loss of muscle tone, particularly of the muscles of respiration, the less effective was the manual method used. The tomograms showed clearly that the diaphragm scarcely moved at all during the procedure and the movement of the chest wall was inadequate for good ventilation. This situation is held to be valid for all the usual manual methods of artificial respiration whether they be carried out in the prone or supine position.

It is to be regretted that the Schafer method was not tested in this manner as this method is directed particularly towards movement of the diaphragm.

It was further shown that even relatively light insufflation with an anaesthetic bag would produce adequate enlargement of the chest cavity and sufficient movement of the diaphragm to give a satisfactory ventilation.

From these experiments it was concluded that the greater the loss of muscle tone in asphyxia, the more rapidly must resort be made to positive insufflation of air or oxygen, otherwise a serious disturbance in the gaseous exchange will supervene leading to hypoxia, anoxia and a rapid increase in blood carbon dioxide tension. A shadow of doubt is cast on the statistics of successful cases of resuscitation by the manual methods but it may well be that the state of muscle tone in these cases was little removed from normal. It is a matter for conjecture whether more fatalities could have been avoided, where the muscle tone may have been seriously impaired, by using other methods than the conventional manual techniques.

The relative inefficiency of the manual methods, which increases with the depth of asphyxia, requires that a better method be introduced, *e.g.* a method of direct, rhythmic insufflation of air or oxygen. Recent literature is cited and it is suggested that the mouth-to-mouth technique should be developed so that its aesthetic and hygienic disadvantages are overcome. Experiments carried out in America are quoted where a tidal volume of between 1,000 and 2,000 cc. of air was insufflated into an apnoeic volunteer at a rate of 12 times per minute and this was maintained without difficulty for 30 minutes. When the blood oxygen saturation had been permitted to drop to 88% in the apnoeic subject, 5 direct exhaled air insufflations were sufficient to return it to normal (98–100%).

The manual methods are of little value where the victim has emphysema since it is not possible, in such cases, to expand the thoracic cavity sufficiently to permit adequate ventilation. *L. M. Croton*

Ulmer, W. T., Ey, W., Herberg, D., Reichel, G. & Schwab, W. Untersuchungen über die Wirksamkeit manueller Beatmungsmethoden. [**The Effectiveness of Manual Methods of Artificial Respiration**] *Deut. med. Woch.* 1960, Jan. 8, v. 85, No. 2, 58–62, 90–91, 7 figs. [27 refs.]

Most workers attempt to evaluate methods of artificial respiration by measuring the tidal volume produced but this concept is now being treated with reserve since it is the extent of alveolar ventilation which is of greatest importance for resuscitation. Non-uniform ventilation of the lungs may lead to an increase in the functional dead space so that normal or even supra-normal tidal air volumes may not ensure the maintenance of normal blood gas values.

The methods of Thomsen, Holger-Nielsen and Silvester-Brosch were tested on completely relaxed subjects while continuous records were made of arterial blood oxygen saturation and alveolar carbon dioxide tension. The tidal air volumes, respiration rate and energy expenditure of the operator were also recorded. 2 series of tests were carried out (i) on intubated subjects (ii) on non-intubated subjects.

The experimental results showed that, in conditions of deep unconsciousness, insufficient alveolar ventilation was obtained with all techniques tested without actively maintaining the airway patent. Full retraction of the subject's head and drawing the jaw forward produced a marked improvement. Comparative tests on intubated subjects have little practical value since an airway is rarely available in an emergency. Reference is made to the pioneer work of Safar who obtained mean tidal air volumes of 654 cc. using the Holger Nielsen method and 503 cc. using the Silvester method on completely relaxed, intubated subjects but both methods produced only around 130 cc. tidal volume on non-intubated subjects.

The manual methods of artificial respiration are subject to several limiting factors which are avoided by the use of the technique of direct insufflation of exhaled air from the rescuer to the asphyxiated victim. The technique is simple to learn, is reliable for ensuring adequate alveolar ventilation and produces such rapid results that the rescuer is not unduly fatigued.

L. M. Croton

Ulmer, W. T., Ey, W., Herberg, D., Reichel, G. & Schwab, W. Untersuchungen über die Wirksamkeit der Mund-zu-Mund-Beatmung. [**The Effectiveness of Expired-Air Artificial Respiration (Mouth-to-Mouth Breathing)**] *Deut. med. Woch.* 1960, Jan. 8, v. 85, No. 2, 63–7; 91–2, 4 figs. [22 refs.]

Recent experiments have tended to discount the value of the conventional methods of artificial respiration. One of the major objections to the recently advocated method of direct mouth-to-mouth insufflation of air is the possibility of the "hyperventilation syndrome" occurring in the rescuer.

Experiments are reported where this possibility was tested and suggestions made whereby it could be avoided.

Immediately before surgical operation, 7 male and 2 female patients were completely relaxed with suxamethonium after intravenous pentothal anaesthesia. Direct mouth-to-mouth, or mouth-to-airway insufflation was carried out for 6 minutes with the same beneficial results noted in earlier papers. Measurements of blood oxygen saturation and carbon dioxide tension were

made on the patients while the operator's own carbon dioxide tension was similarly observed and recorded.

The "hyperventilation syndrome" occurs when the alveolar carbon dioxide concentration decreases to between 2–3% (*i.e.* 15–22 mm. Hg) but, in healthy persons, this would correspond to an increase of 150–300% in the respiratory minute volume which is quite unnecessary for the correct application of the direct insufflation technique. Lay persons should be taught to recognize the symptoms of hyperventilation so that remedial measures such as a short pause in insufflation may be taken.

A respiratory technique for the rescuer is suggested where he inspires quickly and deeply then exhales immediately into the victim. Such a technique would prevent intimate mixing in the alveolar dead space so that the air blown into the asphyxiated casualty would more nearly approximate to the constitution of normal atmospheric air.

An oro-nasal mask (Resutator) adapted for artificial respiration is described. The device consists of the usual oro-nasal mask with 2 valves. One valve permits entry of fresh air for the rescuer and the other permits expiration by the casualty. There is a "dead space" of 150 cc. between the fresh air inlet valve and the rescuer's mouth-piece which permits a richer air mixture to be blown into the casualty. *L. M. Croton*

Ulmer, W. T., Harrfeldt, H. P. & Reichel, G. Die Durchführung der verschiedenen Mund-zu-Mund-Beatmungsmethoden. Atemspende. [**A Comparison of Different Methods of Expired-Air Artificial Respiration by Donor**] *Deut. med. Woch.* 1960, Jan. 8, v. 85, No. 2, 67–70, 92, 6 figs. [10 refs.]

The term "blood donor" is now well known and it is suggested that to counteract any prejudice, the operator using the "mouth-to-mouth", "mouth-to-nose" or "mouth-to-airway" technique of artificial respiration be called a "breath donor".

These 3 techniques have been used on 8 completely relaxed subjects and comparative records made of arterial blood oxygen saturation and alveolar carbon dioxide tension in an attempt to determine the most appropriate method of direct "breath donation" by lay rescue personnel, and to lay down a drill for its performance.

Any foreign bodies are rapidly removed from the mouth; in the case of drowning, the pelvis is raised to empty fluid (taking no more than 30 seconds) and the casualty placed in the correct position with the head fully retracted as soon as possible. The rescuer adopts the most convenient position to perform either of the techniques and commences insufflation immediately. The gaseous exchange in all 3 methods tested was approximately the same and the "donor" was in a good position to observe the effects of his direct insufflation. If the casualty's head is not retracted sufficiently, air pressure may open the oesophagus and air may enter the stomach; this is avoided by correct positioning.

Tests were made to determine how long a rescuer could interrupt the procedure if the symptoms of hyperventilation were detected. A maximum of 30 seconds are available for a pause in insufflation during which time the rescuer could call for assistance, cleanse air passages or change his posture before the casualty's arterial blood saturation shows a serious decline.

The disadvantages of mouth-to-mouth insufflation are considered to be (i) the difficulty of sealing the mouth completely and (ii) operator fatigue caused by maintaining the casualty's mouth open and at the same time retracting the head.

The mouth-to-nose technique is preferred since the posture adopted by the rescuer is less rigid; the hands and arms are in a relatively natural position and it is easy to seal the casualty's nose completely with the mouth.

Avoidance of aesthetic and hygienic objections is claimed by using the mouth-to-airway technique but it is emphasized that, in lay hands, an airway is potentially dangerous. A rescue airway is described which consists merely of a rubber mouthpiece with an extremely short tube and a strap for affixing it to the neck. It is claimed that such an airway is the simplest and most hygienic method of carrying out artificial respiration by direct insufflation even when the patient is being transported to hospital.

Although no time should be lost in instituting artificial respiration, it is preferable to get the patient off the ground on to a table or similar structure since this effectively reduces postural fatigue on the part of the operator. *L. M. Croton*

OCCUPATIONAL DISEASES

Leach, S. J. & Walker, G. L. **An Underground Investigation of the Distribution of Respirable Dust from Continuous Operations and from Shotfiring simulated by Nitrous Oxide as a Tracer Gas.** Reprinted from *Trans. Inst. Mining Engineers.* 1959–60, v. 119, Pt. 2, 107–23, 9 figs. Discussion 123–4.

Dust particles of sizes causing pneumoconiosis move only very slowly relative to the air in which they are suspended, hence the spread of dust from a source into the current of air travelling through a mine can be inferred by releasing gas and measuring its concentration downwind, the gas being more amenable to experiment than dust. Nitrous oxide, diluted with air to lower the density, was chosen as a tracer gas because it was easy to estimate and samples could be kept without loss.

The gas was released on a coal face from shot holes through an imitation drill, from near the picks of a rotary coal-cutting machine and from the centre of a ripping lip, again via an imitation drill. Perspective drawings show the location of the numerous sampling positions associated with each release.

Release from the shot hole resulted in a plume of gas passing to leeward with little mixing so that large fluctuations of concentration were observed. The coal cutter, however, produced turbulence in the air which caused rapid mixing and smoothed out concentration gradients. The ripping lip itself gave rise to a large vortex of air which also caused rapid mixing.

Further experiments simulated the sudden release of a pulse of dust, such as would be occasioned by firing a shot; this was done by bursting balloons filled with gas. In fully turbulent flow the peak of the pulse travels at air speed, while the pulse gradually spreads. In the absence of sufficient turbulence the pulse lagged behind the air stream and it was shown that 20 minutes might elapse before the pulse would be cleared from a heading of 120 ft. *C. N. Davies*

MICZEK, G. Vergleichende Untersuchungen an Zyklonentstaubern. [**Comparative Studies on Cyclone Dust Removers**] *Staub*. Düsseldorf. 1960, Jan. 1, v. 20, No. 1, 9–13, 14 figs.

The English summary appended to the paper is as follows:—

"This article comprises a report on investigations of four different cyclone dust removers which were carried into effect under comparable conditions. After a few fundamental observations on the subject of a dust removal by centrifugal force, there follows a thorough description of the construction of cyclones and the testing method. The results of measurings of the precipitation degree with varying pressure losses show satisfactory conformity."

NATIONAL COAL BOARD. **Medical Service. Annual Report 1958** [ROGAN, J., Chief Medical Officer]. 18 pp., 1 diagram. [1959.] London: Hobart House, Grosvenor Place, S.W.1.

At the end of 1958 the National Coal Board employed 79 doctors, including 4 engaged on medical research. Ancillary staff comprised 379 nurses and 2,455 medical room attendants, of whom 907 were full- and 1,548 part-time (medical room volunteers). The general pattern of the work was the same as in previous years but for various reasons there was a change in the emphasis. Thus curtailment of recruitment resulted in a marked fall in the number of pre-employment examinations. Of 16,456 juveniles examined, 85·4% were passed as fit for all types of mining employment, 11·6% fit for restricted employment and 3% were unfit and rejected for employment. These percentages are almost identical with those of 1957 when there were 20,870 examinees. At the end of the year the scheme for the periodical radiographic examination of all mineworkers commenced. The purpose of the scheme, the broad plan of which was described in the report for 1957 [this *Bulletin*, 1959, v. 34, 341], is to X-ray all mineworkers regularly at intervals of 5 years. Participation by workmen is voluntary but managements and unions have co-operated with the result that the target of 80% response might well be surpassed. To carry out the examinations it has been necessary to design and equip special mobile X-ray units, of which there are 9. The specification of these is set out and illustrated in an appendix to the report.

The first-aid and ambulance services are maintained by 21,214 officials and 14,787 men who passed a first-aid examination within the last 3 years. These figures represent an increase of 3,929 and 2,090 respectively over 1957. The Morphia in Mines Scheme continued to operate satisfactorily.

Periods of Benefit for beat diseases, dermatitis and nystagmus showed a slight rise in 1958 thereby interrupting the downward trend of the previous 4 years.

New certifications for pneumoconiosis declined by 854, from 3,756 in 1957 to 2,902 in 1958. Dr. Rogan states that the reason for this fall is uncertain. [Statistics published since in the Digest of Pneumoconiosis Statistics for 1958 show that the decline was not general throughout the 9 colliery divisions; increases occurred in East Midlands and South Western (mainly South Wales) divisions; the West Midlands division, chiefly the North Staffordshire area, accounted for no less than 621 (72·8%) of the 854 cases.] The following warning is so important as to justify quotation:

"It was emphasized in the 1957 report that too much weight should not be placed on these certification figures for pneumoconiosis and this point must be reiterated. It is expected that the periodic x-ray scheme for mineworkers will result in an appreciable rise in the number of cases diagnosed by the Ministry of Pensions and National Insurance during 1959 and the succeeding four years. Such a rise will not signify that more men are developing pneumoconiosis than previously, only that most of the existing cases are being brought to light." *A. Meiklejohn*

NATIONAL COAL BOARD. **Medical Service. Research on Medical and Allied Problems. Annual Report 1958** [ROGAN, J., Chief Medical Officer]. 12 pp. [1959.] London: Hobart House, Grosvenor Place, S.W.1.

The medical Service of the National Coal Board continued during 1958 to promote and maintain an extensive programme of research into medical and allied problems, which affect the safety and health of coalminers.

The major projects included: *Pneumoconiosis Field Research*, National Coal Board; *Lung Function in Pneumoconiosis*, Queen's College, Dundee; *The Causation of Complicated Pneumoconiosis*, Post-Graduate Medical School, University of London; *Beat Diseases*, University of Sheffield; *The Prevention of Epidermophytosis*, National Coal Board; and *Research on Hot and Humid Conditions*, University of Oxford.

In addition several statistical studies were undertaken into sickness and accidents among miners. As previously the work, wherever carried out, was under the supervision of 4 panels of experts; epidemiology, industrial medicine, physiology and psychology. The purpose of the report is simply to record work in progress without entering into details. Where the work has been

published the references are given. [For 1957 Report, see this *Bulletin*, 1959, v. 34, 342.] *A. Meiklejohn*

BERGMAN, I. & GORDON, R. L. **The Composition and Pathogenicity of Airborne Dust in British Coalmines.** Reprinted from *Geol. en Mijnbouw.* (n.s.) 1959, Sept., v. 21, 329–34, 2 figs. [36 refs.]

In British coalmines emphasis in the control of dust has so far been placed mainly on the quantity of airborne dust of respirable size. This is substantially true although the recommended "approved dust conditions" distinguish between coal, anthracite and rock (quartz). Instruments used in dust control investigations have been designed and used for their efficiency to determine the number of particles of various sizes in the air. In conjunction with dust counting the Pneumoconiosis Field Research (25 pits scheme) teams in Britain have made thorough studies of the composition of the rocks and other strata in which the coal occurs. So far compositional analyses of airborne dust have not been undertaken as a routine measure. That there is need for such analyses is underlined by a few studies, which have suggested that the composition of the airborne dust may differ substantially from that of the minerals from which the dust derived. The subject is now receiving greater attention as suitable instruments and methods, such as X-ray powder diffraction, become more generally available.

The value of increased numbers of samples is likely to be two-fold. In the first place, if airborne-dust samples can be obtained for compositional analysis in sufficient numbers to enable comparisons to be made with the incidence of disease in various places and conditions, considerable advances may in time be made. Secondly, it may be possible to provide a sound foundation by means of which the composition of airborne-dusts may be not so much measured as deduced from analyses of such other materials as run-of-mine coal and rock strata. *A. Meiklejohn*

ISHIKAWA, A. [**Studies on Silicosis. IV. Histological Change of Rabbit Lungs by Intratracheal Injection with Hydrous Silicic Acid (Vitasil) and an Investigation of the Toxicity of Vitasil-Mixed Feed**] *Japanese J. Nation's Health.* 1959, Sept., v. 28, No. 3, 537–49, 30 figs. [In Japanese.]

The English summary appended to the paper is as follows:—

"A preparation of 3 cc of the Ringer's solution to which 250 mg of hydrated silicic acid (Vitasil) had been added was injected into the trachea of rabbits, and the lungs and the thorax lymphatic glands of these rabbits were histologically investigated. For making the control, 250 mg of α-quartz was injected into the trachea of rabbits. And the feed containing 6 mg of Vitasil per 3 g stuff was given to mice once a week, and the subsequent toxicity was examined.

"(1) 15 rabbits were divided into three groups of 1-month, 3-months and 6-months on the basis of the feeding period. For the sake of the control, 6 rabbits were grouped likewise. 40 mice were divided into three groups of 1-month, 3-months, 6-months, and the control group.

"(2) Autopsy findings evidenced that no marked difference was found in Vitasil and α-quartz administrations.

"(3) Histologically the subjects injected with Vitasil were discovered to have had an inflammative response produced by the foreign body in the lungs and the lymphatic glands. But neither the production of fibroblast nor the tendency of progressive fibrosis was found.

"(4) α-quartz administered rabbits demonstrated the stronger inflammative response as compared with the subjects with Vitasil. Particularly in the lymphatic glands the production of reticular cells and the tendency of progressive fibrosis were notable.

"(5) In the toxicity, it was observed that the livers, the kidneys and the spleens of the non-control group did not differ greatly from those of the control group, but these were quite normal. Vitasil seemed not to be absorbed through the intestinal canals."

RONDEZ, R., RÜTTNER, J. R. & ANDERS, G. Mastzellreaktion nach Einwirkung von Quarz in isotoner und nicht isotoner Suspension im Intraperitonealversuch bei der Maus. [**Mast Cell Reaction after the Action of Quartz in Isotonic and Non-Isotonic Suspensions Injected Intraperitoneally in Mice**] Reprinted from *Med. Exper.* Basle. 1959, v. 1, No. 1, 33–7.

The English summary appended to the paper is as follows:—

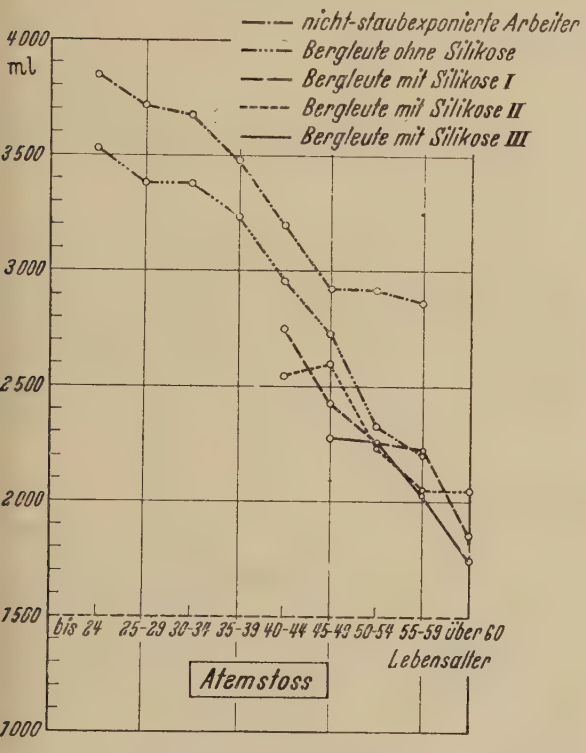
"Fine-grained quartz powder suspensions in aqua dest. and/or isotonic saline, when injected intraperitoneally, produced a distinct mast-cell degranulation in the mesentery of the mouse. The mast-cell degranulation is an immediate reaction. No strict dependence of the degranulation effect on the suspension-medium was established. The mast-cell degranulation also occurred when a quartz-free suspension-medium was used. It is more pronounced with aqua dest.

"Attention is drawn to the significance of these findings for experimental silicosis research."

WORTH, G., GASTHAUS, L., LÜHNING, W., MUYSERS, K., SIEHOFF, F. & WERNER, K. Lungenvolumina und Lungenzeitvolumina bei Koh'enbergarbeitern. [**Lung Volumes and Ventilatory Capacity in Coal Workers**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 4, 396–419, 12 figs. [16 refs.]

In a previous paper [this *Bulletin*, 1956, v. 31, 1016] WORTH and his colleagues studied the effect of occupational dust exposure on lung function in coal-miners by clinical and physiological examinations before, during and after a 6-hour shift. No significant changes were observed. In this paper they consider the effect of long-term dust exposure by investigating 1,521 coal-miners and comparing them with 240 men engaged in equally heavy non-dusty work in other industries. 750 of the miners were capable of heavy work and free

from silicosis; 173 had Stage I, 361 Stage II and 237 Stage III silicosis. There were 30 non-miners and 100 miners without silicosis in each 5-year age group, except in the 20–24 in which there were only 50 miners. Lung volumes (total lung volume, vital capacity, functional residual and residual capacities) and ventilatory capacity (direct maximum breathing capacity and forced expiratory volume) were measured and the results are presented in great detail for each test in a number of tables and diagrams. The importance of age is clearly evident and the mean results have been given for each 5-year age group from 20–64 years.



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Average Values of Ventilatory Capacity in Workmen not exposed to Dust and in Miners with and without Silicosis: in Age-Groups.

At all ages lung function was lower in the miners without silicosis than in the men not exposed to dust and differences, statistically significant at the 1% level, were found between the 2 groups in the 20–39 and 50–64 but not in the 40–49 age groups (see figure showing the forced expiratory volume). The smaller differences in the middle-aged groups are explained by assuming that those miners who were affected soon after starting work have left the industry.

The mean values of the lung function tests were in general slightly lower in the miners with silicosis than in those without, and in those with Stage II and III silicosis reached statistical significance on some of the tests in the 40–49 age-group. The difference in lung function between miners and non-miners is attributed to the dust exposure of the former group, and the experiments of SCHILLER (*Wiss. Forschungsberichte*, 1958, v. 66, 435, 474) who demonstrated hyperplasia and hypertrophy of goblet cells and atrophy of the mucous membranes in dogs kept underground for 6 years, is cited to support this view.

The relation of lung function to dust exposure is then considered in 630 men without silicosis, aged 25–60 years. There was a slight overall decline in lung function with increased duration of underground work and this was most clearly demonstrated by the ventilatory capacity measurements which showed significant decreases with increased dust exposure in the 25–34 and 45–49 age groups.

In conclusion the age at entry into mining is considered and though no clear picture emerged, differences in residual and functional residual volume between the mining and non-mining groups were larger in those entering mining early in life.

[This is an important paper which should be read by anyone interested in this subject. Unfortunately the method of selection of subjects is not stated. The distribution of the men with silicosis, however, suggests that this was not a working population, but that miners attending hospital or applying for compensation must have been included and the probability of bias from inclusion of such men must make the validity of some of the conclusions questionable. Nor is it clear how the equal numbers in the different age-groups were obtained.] *I. T. T. Higgins*

CARINI, R. L'urobilinuria nella silicosi polmonare. (Reperto patologico o riscontro casuale?) [**Urobilinuria or Pulmonary Silicosis. (Pathological Sign or Casual Finding?)**] *Acta Med. Legalis et Socialis*. Liège. 1959, Jan.–June, v. 12, Nos. 1/2, 39–42. French summary.

It is particularly difficult to confirm or exclude the early stages of silicosis in workers who, having a history of long-standing exposure to the silica hazard without any clinical signs or symptoms, show a pattern of X-ray shadows which may be equally due to a "reticular fibrosis" or to the medium-sized bloodvessels.

Carini reports on his experience in the routine examination of 434 miners of pyrites and lignite in the Grosseto area, seen between 1st January 1954 and 30th June 1955 on account of claims for industrial compensation. Besides going into the clinical aspects of each case, the investigation included X-rays, often stratigraphic [tomographic], ECG, blood counts, sedimentation rate, sputum and urine tests and intradermal reaction tests.

No evidence of silicosis was found in 118 of these subjects and 129 others showed some of the manifestations of initial silicosis without having reached a stage which satisfied the conditions which entitled the worker to compensation. The other 187 subjects in this series had developed silicosis to a stage for which compensation was provided.

The urine of 33 subjects, gathered in the previous 12 hours, contained an excess of urobilin and they were all from the second group referred to above, namely, the 129 workers with initial silicosis. None had any history pointing to digestive or other abdominal trouble and they had been working in the mines for periods of 15 to 30 years. Some 60% of these 129 workers, with signs of initial silicosis, showed a slight enlargement of the liver with no tenderness or appreciable hardness. The urobilin test was positive in only 3 cases from the first group and 7 from the last group. An excess of urobilin in the urine may, therefore, be a useful sign of incipient silicosis in those exposed to the hazard. *J. Cauchi*

GIULIANI, G. Poliadenopatia ilare e mediastinite sclerotica adenopatica nella silicosi polmonare. Ulteriori contributi anatomoradiologici. [**Hilar Polyadenopathy and Adenopathic Sclerotic Mediastinitis in Pulmonary Silicosis. Further Anatomical and Radiological Contributions**] *Acta Med. Legalis et Socialis.* Liège. 1959, Jan.–June, v. 12, Nos. 1/2, 43–8.

Giuliani is consultant radiologist to big steelworks in Terni, administrative centre of the Province of Umbria, Italy. He finds that exposure to the inhalation of silica dust leads to an early enlargement of the hilar glands which receive the inhaled material through the pulmonary lymphatics: he describes the resulting shadows which are revealed by lateral radiography in such cases. Loose adhesions form, in due course, between these hilar glands and the mediastinal wall and, later, a mediastinitis may develop. To illustrate these processes, Giuliani has selected, and reported on, the cases of 3 steel workers who worked in the foundry and handled material with a large proportion of silica dust. One of these workers died in a road accident at the age of 32 after having worked in the steelworks for 5 years. The second subject died of a myocardial infarction at the age of 58, after an exposure of 12 years to the silica hazard. The other subject succumbed to pulmonary silicosis at the age of 66: he died 5 years after having given up the work which had exposed him to the silica hazard for 34 years.

Besides his first-hand knowledge of the X-ray history of these 3 workers, Giuliani had the opportunity of being present at their post-mortem examination and of following up the subsequent histological investigations.

This paper stresses the practical importance of detecting this polyadenopathic sign of incipient silicosis because of the preventive value of removing the worker from further exposure to the hazard on the appearance of this danger signal and before irreversible, parenchymatous changes in the lung have appeared.

J. Cauchi

FERRARIS, A. & PAOLI, G. Il quadro broncoscopico della silicotubercolosi. [**The Bronchoscopic Picture in Silico-Tuberculosis**] *Lotta c. la Tubercolosi.* 1959, July–Aug., v. 29, Nos. 7/8, 1021–30. [25 refs.]

In this paper the authors give 3 schematic outlines to show what are the likely, sometimes alternative, details which may be seen through the bronchoscope in cases of silicosis, broncho-pulmonary tuberculosis and silico-tuberculosis respectively. The tracheo-bronchial lesions which may be found to affect the picture seen in respiratory tuberculosis are also schematically listed according to 2 separate authorities.

It is obvious that the many lesions may combine in a wide variety of patterns in each of these 3 diseases and so may the signs to be seen throughout the bronchoscope. No pattern or patterns can be expected to be typical of silico-tuberculosis, but a bronchoscopic examination can, nevertheless, prove of great value in the diagnosis of this condition and this is illustrated by a series of 6 cases of which the authors give notes and photographs at the end of another paper on bronchography [see below]. *J. Cauchi*

FERRARIS, A. & PAOLI, G. Il quadro broncografico della silicotubercolosi. [**The Bronchographic Picture in Silico-Tuberculosis**] *Lotta c. la Tubercolosi.* 1959, July–Aug., v. 29, Nos. 7/8, 1031–50, 13 figs. [22 refs.]

As in their paper on bronchoscopy [see above], Ferraris and Paoli set out 3 schematic outlines of the likely bronchographic signs to be seen in cases of silicosis, broncho-pulmonary tuberculosis and silico-tuberculosis respectively. From another authority they quote a list of the signs which may be observed when tuberculosis involves the bronchial system. The signs will combine in many different ways to give a wide variety of bronchographic shadow patterns none of which can be said to be typical of silico-tuberculosis, but bronchography can still be of great value in diagnosis.

The authors have carried out both bronchoscopic and bronchographic examinations on 27 patients found to be suffering from silico-tuberculosis and they select 6 of these to describe their findings and conclusions in each case, reproducing photographs of the bronchography and of the chest radiography. Both bronchoscopic and bronchographic pictures in 1 of these cases showed the signs of silicosis but did not show any evidence of the associated tuberculosis at the time. In 2 other cases, both bronchoscopy and bronchography gave indications of the tuberculous association, while in 2 other cases the indications were seen by bronchoscopy but not by bronchography and in the other case it was the opposite. *J. Cauchi*

VIGLIANI, E. C. & SASSI, C. La cura della tubercolosi attiva nei silicotici. [**Treatment of Active Tuberculosis in Silicotic Subjects**] *Med. d. Lavoro.* 1959, Oct., v. 50, No. 10, 593–7. English summary.

Between September 1955 and September 1958 the authors treated in the famous Clinic of Industrial Medicine of Milan University 85 patients who had both silicosis and active tuberculosis, divided as follows: 41 had micro-nodular or nodular silicosis, and 44 had conglomerate or massive silicosis. 81 patients had 1 or more tuberculous cavities, but in 4 who were sputum positive, no cavity could be seen even after tomography.

5 different schemes of treatment were used in which isoniazid was combined with streptomycin, PAS, pyrazinamide, or cycloserine. Favourable results were only obtained in patients with recent tuberculosis who had not too advanced silicosis, while in those with more advanced silicosis and with extensive or multiple cavitation the results were quite frequently nil.

In general isoniazid + streptomycin, or isoniazid + pyrazinamide are indicated in recent tuberculous infections and isoniazid + PAS in high doses, or isoniazid + cycloserine in cases tending to become chronic who probably have had treatment with antituberculous drugs for long periods previously. In patients with signs of tuberculous toxaemia the addition of prednisone was often very valuable, though steroids are dangerous in those with advanced cavitation. The authors consider that pneumothorax is only useful in the initial stage of silicosis. They emphasize that patients with the combined disease must be treated for long periods under strict medical supervision, so that if one combination of drugs proves ineffective, another may be tried. They are convinced that patients with the combined disease even when reasonably stabilized clinically should still continue treatment for 1–2 years as any interruption is likely to lead to rapidly evolutive tuberculosis. Patients with evolutive or serious silicosis must be considered as being especially sensitive to the tubercle bacillus by reason of the fact that the macrophages having ingested the quartz particles liberate polysaccharide substances which are endotoxic [the work on which this opinion is based is to be published later]. *W. K. Dunscombe*

DESOILLE, H. Étude critique de la réparation de la silicose. [**Critical Study of Compensation for Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1959, Nov.–Dec., v. 20, No. 6, 741–50.

In France legislation covering compensation for silicosis was first enacted in 1945. Since then various provisions have been amended and extended to conform to current experience. Medical and administrative difficulties continue to arise and attract criticism and complaint. At a conference on 23 February 1959 by request of the Department of Social Insurance, Paris, Professor H. Desoille critically reviewed the subject of compensation for silicosis in France. Introducing his paper he described briefly the history of silicosis as an occupational disease. He then traced the development of compensation for the disease between 1945 and 1958. While admitting that considerable advance had been made during this period, he underlined certain problems which were still outstanding and called for their remedy. [The difficulties which Professor Desoille emphasized are not peculiar to French silicosis compensation legislation which appears to be rather behind comparable legislation in Great Britain. It would appear (pp. 751–52) that the Department of Social Insurance proposes to review the existing law, for, at a subsequent meeting of the Society of Occupational Health and Hygiene on 25 May 1959, it was agreed to set up a committee to study the question.]

A. Meiklejohn

COCHRANE, A. L. & CARPENTER, R. G., with the assistance of F. MOORE. **Investigation into the Working of the "Death Benefit" for Coalworkers' Pneumoconiosis.** *Brit. J. Preventive & Social Med.* 1959, July, v. 13, No. 3, 128–30.

[Under the National Insurance (Industrial Injuries) Act, 1946, death benefit is payable to dependents whose claim is admitted that the death of the workman has been caused by pneumoconiosis or pneumoconiosis accompanied by tuberculosis. The duty of certification is restricted to the Pneumoconiosis Medical Panels of the Ministry of Pensions and National Insurance. In reaching their decision they have in most cases information derived from a post-mortem examination. Nevertheless it is not always easy to decide the cause of death. Pneumoconiosis is a chronic disease in which many patients die of intercurrent unrelated conditions. This means that there is a distinction between those who die from and those who die with pneumoconiosis. Again it is not generally understood that the Pneumoconiosis Medical Panels interpret the phrase "caused by" as including those cases where death has resulted from concomitant extraneous disease but in their opinion has been materially accelerated by or substantially contributed to by pneumoconiosis. In cases where there is reasonable doubt it is the practice of the panels to exercise this in favour of the dependents. Despite this generous approach individual claimants who fail to get a favourable certificate are aggrieved and institute an appeal to the Commissioner.]

Cochrane and his colleagues considered that the matter justified a quantitative investigation if suitable material could be found. This existed in the records of the Rhondda Fach enquiry, where in the year 1950–51, 659 miners and ex-miners were discovered suffering from coal-workers' pneumoconiosis in the advanced categories of progressive massive fibrosis (PMF), B, C, and D. The history of these cases was traced over the succeeding 6 years. The number of deaths observed was 192 whereas on the basis of the Registrar General's death rates for all males at various age-groups in England and Wales only 111 were expected. The authors postulated certain assumptions. On this basis they were able to calculate the number of certificates attributing death to the disease which might be expected, and to compare these with the number actually observed. The conclusion is that in the South Wales area the Pneumoconiosis Medical Panel was generous in favour of the dependents.

[This finding confirms what is fairly well recognized and indeed what would be expected in the circumstances recorded in the introduction to this abstract (above). The real pertinent problem remains unanswered, namely, how should one certify the cause of death in cases of bronchitis and emphysema in which simple pneumoconiosis is present? Is death due to pneumoconiosis, which entitles the dependents to industrial benefit and associated advantages, or is it due to bronchitis and emphysema and so entitling the dependents only to the lower rates of death benefit under the National Health Service?] *A. Meiklejohn*

MESSITE, J., REDDIN, G. & KLEINFELD, M. **Pulmonary Talcosis, a Clinical and Environmental Study.** *Arch. Indust. Health.* Chicago. 1959, Nov., v. 20, No. 5, 408–13, 4 figs.

In 1940 a chest X-ray survey of 221 talc miners and millers employed at several plants in St. Lawrence County, New York, disclosed pulmonary fibrosis in 32 workers, 18 of whom had no other dust exposures. The pneumoconiosis was of the fibrogenic type. Dust conditions at this period were very bad, varying between 2 million particles per cubic foot in mucking and 2,800 million particles per cubic foot in drilling. An intensive engineering programme to diminish the dust hazard was instituted between 1943 and 1948. From 1954 to 1958 a further study was undertaken to evaluate the effects of these preventive measures. At the same time a similar investigation was made at a talc plant in Lewis County, New York.

The investigations comprised occupational and medical history, physical examination, chest radiography by means of a transportable 70 mm. photofluorographic chest unit, chemical and physical analyses of the different varieties of talc and dust and dust counts at separate working places. At the mines in St. Lawrence County the talc was tremolite and had a fibrous structure, whereas the talc in the plant in Lewis County was composed of granular or scaly particles, which were non-fibrous.

The findings indicated that both types of talc can produce pulmonary fibrosis; the fibrous or tremolite variety is the more pathogenic.

At the St. Lawrence mines and mills great improvement had been achieved in the control of the dust hazard, notably by the introduction of wet drilling. This was reflected in a lower incidence of pulmonary fibrosis among the miners. Although the incidence of pulmonary talcosis among the millers had not appreciably changed, the severity and progression of the disease diminished. *A. Meiklejohn*

MINISTRY OF LABOUR & NATIONAL SERVICE. **Joint Standing Committee on Safety, Health and Welfare Conditions in Non-Ferrous Foundries. Second Report.** pp. iv + 24. [20 refs.] 1959. London: H.M. Stationery Office. [1s. 9d.]

The Joint Standing Committee presents the report of its Technical Sub-Committee with an Appendix on health aspects of non-ferrous foundry processes by W. D. BUCHANAN.

The report of the Technical Sub-Committee falls under 5 headings: general considerations, dust, fumes, other health precautions, and conclusions.

The need for keeping the amounts of dust and fume to a minimum is emphasized. Dust and fume should be eliminated if possible, controlled at source if elimination is impossible, and dealt with by general ventilation only if local control is impracticable. In the latter event it may be desirable to segregate particular processes. Dust from dressing processes can often be reduced by careful attention to the sequence of operations. Castings (other than die castings) should not be given to dressers until they have been treated in some form of mechanical blasting equipment. Wire brushing should not be done without local exhaust ventilation.

For the prevention of fume, temperatures of molten metal should be kept as low as possible. Some alloys fume as they are being cast. Hence, the shorter the distance that these fuming ladles have to be transported the better.

The topics discussed in the Appendix include pneumoconiosis, metal fume fever, lead fumes, other metal fumes, health aspects of fluxes and de-gassing, the carbon dioxide process, shell moulding, the possible effects of the foundry environment on certain diseases, heat exhaustion, and first aid. Some of these hazards are well known in foundries, and must be countered. The effects of some others have not been seen in foundries, and in the view of the Sub-Committee they never will be if founders understand the risks and act accordingly.

It appears that there may be more pneumoconiosis in non-ferrous foundries than has been supposed in the past [this *Bulletin*, 1955, v. 30, 780], and this possibility makes it all the more important that great care should be taken in the suppression of dust. The Sub-Committee makes specific reference to the hazards due to fumes of zinc, lead, beryllium, cadmium, phosphorus, selenium, tellurium and chlorine.

Commenting on the reference to heat exhaustion, the Sub-Committee agrees that saline drinks should be provided where there is much exposure to heat, but expresses the view that the best approach is to use furnaces of higher fuel efficiency which would dissipate far less heat.

[For the first Report, see this *Bulletin*, 1957, v. 32, 761.] *Thomas Bedford*

KEATINGE, G. F., BUXTON, E. R. & HUNT, P. J. **A Study of the Incidence of Bronchitis amongst some Foundrymen in Derbyshire and Nottinghamshire, compared with a Contrasting Occupational Group, and a Geographical Study of Bronchitis Mortality in the Foundry Workers of England and Wales.** *Brit. J. Dis. Chest.* 1959, Oct., v. 53, No. 4, 333–45. [24 refs.]

Many studies of the incidence of bronchitis among industrial populations have been carried out recently [this *Bulletin*, 1956, v. 31, 39, 1234; 1957, v. 32, 50; 1958, v. 33, 238] but none specifically relate to foundrymen. Advantage was taken of favourable conditions for an investigation into this which existed at the Butterley Company in Derbyshire [see also this *Bulletin*, 1955, v. 30, 144]. A comparison is made between foundrymen and wagon workers who apart from the conditions associated with iron founding are apparently similar in all respects. Only men who had worked for 10 years or more were included. 92 foundrymen and 67 wagon workers were investigated. Details are given of the investigations which appear to have been conducted very satisfactorily. Interviews were carried out by 2 observers who worked independently, and interviewed the same men after an appreciable lapse of time.

It was thought that presumptive bronchitis occurred on 20·6% of the foundrymen and 14·9% of the wagon workers. There was little difference in smoking habits between the 2 sets of workers. The housing conditions were satisfactory and the locality was semi-urban. In both groups a considerable proportion of the men had worked as mine workers and underground. The amount of time lost through respiratory illness by the 92 foundrymen was only an average of 0·44 day per annum but for the wagon workers it was 0·78 day per annum. When the necessary adjustments are made there is little evidence that death was more frequently from respiratory disease in the foundry workers than in the wagon workers. It was concluded that at the Butterley Works the incidence of serious bronchitis was not greater in foundry workers than in wagon workers.

It is estimated that 57% of all foundry worker in England and Wales live in areas having an excess death rate from bronchitis, and it is suggested that it is the geographical situation rather than the occupation that causes the high mortality from bronchitis returned in general for foundry workers and their wives.

F. H. Young

SULLY, A. H., STOCH, C. M. & SLATER, J. M. **The Measurement and Control of Dust in Foundries.** Reprinted from *Brit. Foundryman.* 1959, Apr., 193–211, 20 figs. [44 refs.]

A preliminary dust survey of 13 steel foundries with an Owens counter showed that airborne particles were seldom larger than 5 microns while the median size was about 1 micron. It is argued from this that loss of airborne dust by settlement is small [the argument is supported by a table of falling velocities which much exaggerates the rate of fall]. The results with the Owens counter also showed that the particle distribution was reasonably constant over the 13 foundries and this was used to justify the employment of the Hexhlet mass-sampling instrument in a further study of average dust concentration in a large number of fettling shops. Since the Hexhlet is a selective sampler which has been very carefully designed to record the mass of dust capable of causing pneumoconiosis, whereas the Owens instrument is selective merely by reason of undesirable artefacts, it is extraordinary to find the sanction for using the former determined by the findings of the latter.

2 years' experience with the Hexhlet sampler in 58 foundries revealed dust concentrations between 1·2 and 23 mgm./100 ft.^{3}, with an average of 5·1, and quartz contents from below 1% to 37%, with an average of 6·9%, a figure lower than had previously been observed. The quartz was determined by X-ray analysis and doubts are cast upon earlier work on the grounds that silicates had been returned as free silica. The single chemical analysis which is given contains as total SiO_2 nearly double the X-ray amount for quartz. Only traces of cristabolite were found and no tridymite.

The rest of the paper deals with dust suppression. Methods of fettling steel castings which do not give rise to clouds of quartz-containing dust are enumerated. Powder washing is a process in which the casting is sprayed with iron dust fed through an oxy-acetylene flame. The air-carbon-arc torch strikes an electric arc between the casting and a carbon electrode. Wet sand blasting is used. Chemical and electrolytic cleaning are mentioned.

Local exhaust systems using side extraction are preferred for knock-out and very high air flows are quoted as necessary. The system of extracting air upwards causes dusty air to pass the operator at breathing level. It has been found satisfactory to introduce fresh ventilating air near floor level and extract entirely from the hoods at local points of dust generation.

Important points in the design of exhaust hoods for grinding are detailed and low-volume high-velocity attachments for portable fettling tools are described. An attachment for a pneumatic chisel sucked 7·5 ft^3/minute at 5 inches of mercury. Although these devices gave excellent dust control when operated under the best conditions there was a continual risk of poor performance.

The most important points were the avoidance of handling sand and dust when dry, and the improvement of production methods to yield better strip and cleaner castings which required less fettling. Regular maintenance of ventilating and exhaust equipment was necessary.

C. N. Davies

OSHIMA, M. [**Studies on the Lead Poisoning. Part 3. Experimental Studies on the Urinary Calcium and Lead Excretion in Lead Poisoning**] *Shikoku Acta Med.* 1959, Sept., v. 15, No. 3, 701–10, 7 charts. [41 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"In the present study, observations on symptoms of lead intoxication in rabbits which were injected subcutaneously with lead acetate were described, together with some remarks about the determination of serum calcium level and urinary calcium level, as well as possible significant influences of Ca-EDTA on calcium levels in serum, urine and other organs in case of administration of Ca-EDTA after discontinuing the administration of lead acetate.

"1) No significant changes in serum calcium level and urinary calcium level were demonstrated between the lead administered group and the control group. Even if changes occurred, they seemed to be slight or transitory ones which should be included in a larger physiological fluctuation.

"2) No significant changes in serum calcium level were observed after administration of Ca-EDTA, though transitory increase in urinary calcium level were demonstrated after administration of Ca-EDTA. The rate of increase in urinary calcium level was demonstrated to be 7 mg/24h after administration of 600 mg Ca-EDTA, and 2 mg/24h after administration of 200 mg Ca-EDTA as compared with urinary calcium average level before administration of Ca-EDTA. These increased amounts of urinary calcium, however, were not so much as the amount of calcium administered.

"3) A transitory remarkable increase in urinary lead level was demonstrated after administration of Ca-EDTA, though no significant differences of the increase

were found among the variation in dose of Ca-EDTA. It was also found that no significant differences of lead level in liver and bone were found among the variation in dose of Ca-EDTA."

SWENSSON, A., LUNDGREN, K. D. & LINDSTRÖM, O. **Distribution and Excretion of Mercury Compounds after Single Injection.** *Arch. Indust. Health.* Chicago. 1959, Nov., v. 20, No. 5, 432–43, 5 figs. [20 refs.]

A tracer study with the radioactive mercury isotope ^{203}Hg was undertaken to compare distributions of Hg from 3 mercurial compounds when administered in amounts which would not produce injury. Mercuric nitrate or phenyl mercuric acetate or methyl mercuric hydroxide was injected intravenously, in a dose of 100 μgm. Hg per kgm. The description of the methods includes discussions of possible errors, initial control analyses to counteract some of them and calulations to overcome sources of variation.

After the 3 compounds, serial estimations of Hg are given for 1 month in blood, kidneys, liver and brain from rats, and for 4 hours in blood and urine from dogs. 4 hours after the injections, Hg was measured in liver, kidneys, brain, cerebellum and colon from the dogs. *In vitro* determinations were made in human whole blood and plasma.

The methyl compound was also administered in larger doses to dogs and rabbits. Serial estimations were made in the dogs for 4 hours in blood after 3 or 1 mgm. Hg per kgm., and in the rabbits in whole blood and plasma for 1 hour after 10 mgm. Hg per kgm.; then in the rabbit Hg was measured in liver, kidneys and brain.

In blood the 3 compounds decreased at similar rates. The organic mercurials were largely bound to the erythrocytes, the other being in the plasma.

Urine excretion began immediately after all 3. Concentration and total excretion were less after the methyl compound. After the inorganic compound a high initial content was followed by temporary anuria; the rat tissue serial estimations showed that with these small doses this serious effect was reversible.

In the organs there was accumulation of Hg, all of which was gradually excreted, partly in the urine. Mercuric nitrate and phenyl mercuric acetate were deposited chiefly in the kidneys, whereas methyl mercuric hydroxide was distributed more evenly throughout the body. The colon wall had a high content after mercuric nitrate. In the central nervous system only small and similar amounts of the 3 compounds were deposited. *M. Patricia Fitzsimons*

NOE, Frances E. **Mercury as a Potential Hazard in Medical Laboratories.** *New England J. of Med.* 1959, Nov. 12, v. 261, No. 20, 1002–6. [32 refs.]

This is a special article in which attention is drawn to the hazards of exposure to mercury particularly in physiological and medical laboratories. Control of mercury vapour in industry is well established but the possibility of insidious mercury poisoning in laboratories is insufficiently realized. The problem of control in laboratories is here clearly considered with references to the literature in sections some of which deal with toxic levels of mercury vapour; portals of entry and absorption; excretion and urinary levels; the clinical characteristics of mercury poisoning and the diagnosis. A valuable section also describes some of the errors of technique in handling and storing mercury and personal habits of smoking and eating in laboratories which may be hazardous. The ventilation of laboratories and the points to which attention should be paid in the construction of new laboratories are also considered. *M. E. Delafield*

NOTHDURFT, W. Über die maximale Arbeitsplatz-Konzentration des Quecksilberdampfes. [**The Maximum Working Concentrations of Mercury Vapour**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1959, Nov., v. 9, No. 11, 263–70, 8 figs. [21 refs.]

The maximum allowable concentration of mercury vapour varies from 75 μgm. per cubic metre in England to 100 in the United States and Germany. Observations in the U.S.A. have shown that at 70 μgm. isolated symptoms but no diagnostic syndrome have occurred. 6 different methods of measuring the concentration are described, including the selenium sulphite, ultraviolet, electrolytic, and dithizone methods. Of these the ultraviolet optical procedure is the most rapid, allowing estimation of 1 μgm. per cu.m. in 1 to 2 litres of air in a few minutes.

Of the varied symptomatology the neuropsychic disturbances are predominant, and may appear with a few weeks' exposure to 10 to 20 μgm. Prognosis is good only with young healthy persons. In animal experiments inhalation has proved much more toxic than orai administration. Excretion is slow and there is some retention by the kidneys and especially by the hypophysis.

5 industrial investigations are discussed and their results analysed. 2 in the fur hat industry in America and 1 in Italy and 2 in the thermometer industry. The results of the first 2 in 1937 and 1941 showed that 100 μgm. cannot be taken as the limit below which no cases of poisoning occur; it corresponded to an incidence of 5 to 10%. In the 1941 investigation a rearrangement in tabular form confirmed that the most severe symptoms began in older people exposed to 160 to 230 μgm. per cu.m., that the severity increased sharply with the concentration and that even slight improvement in the working conditions can be expected to be of hygienic value. The lower limit for "borderline" cases appears to be 100 μgm. but even at this level 4% of the workers showed some symptoms, and lower concentrations must be envisaged as hazardous to sensitized persons. In the Italian work [this *Bulletin*, 1953, v. 28, 1065] a level of 100–150 μgm. per cu.m. was found to be safe.

In the thermometer industry the results were similar, but in 1 factory where women were employed they showed a higher incidence of poisoning. In the second, a special feature was a fall in the number of erythrocytes, increasing with the exposure.

Where exposure to mercury vapour is unavoidable, atmospheric concentrations and the health of the workers must be strictly controlled.

Ethel Browning

EVANS, D. M. **Cadmium Poisoning.** [Memoranda.] *Brit. Med. J.* 1960, Jan. 16, 173–4.

Acute cadmium poisoning was recognized from the symptoms in a man aged 60 who attended the medical department a day after he had spent 5 hours cutting scrap metal with a welder's torch. Investigation afterwards showed that the scrap included cadmium-coated materials. There was no exhaust ventilation. Fumes during the cutting had caused irritation of eyes, nose and chest. Later leg weakness, frontal headache and generalized aches developed. That night he felt cold, slept little, sweated profusely and had rapid breathing. Next day at work he complained only of headache and abdominal discomfort. No abnormalities were found at examinations which included chest X-rays—then or later. After 48 hours, breathlessness on walking and tightness of the chest appeared and the malaise and weakness returned, necessitating treatment in bed symptomatically for several days. On the 14th day there remained only breathlessness and tightness. Blood count and urine were normal. Within $4\frac{1}{2}$ weeks all symptoms had gone.

Cadmium fume is very toxic. When the metal is heated, as in welding, the highly irritating fumes of cadmium oxide are formed. Acute poisoning may result in pneumonitis and death from pulmonary oedema or bronchopneumonia. Chronic poisoning leads to lassitude, cough, dyspnoea from emphysema and sometimes to epistaxis, anosmia and renal excretion of a protein of low molecular weight [this *Bulletin*, 1959, v. 34, 1025]. Cadmium-plated articles should not be used in food preparation because of possible gastroenteritis. Local exhaust is necessary where there is danger of fume or dust. The MAC is 100 μgm. per cc.

Cadmium is used: in atomic pile control rods and alkaline earth accumulators; for electronics and coating bearings; as copper-cadmium alloy in power cables and trolley-bus wires; as halides for photography; as the sulphide in pigments for paint and glass and as the oxide for coating luminescent powders—to give a few examples.

M. Patricia Fitzsimons

LIPINSKI, S. Rozmieszczenie selenu w ustroju. [**Distribution of Selenium in the Organism**] *Med. Pracy.* 1959, v. 10, No. 3, 187–98, 7 figs. [66 refs.]

The English summary appended to the paper is as follows:—

"The author has performed the experiments on white rats. He investigated the selenium (Se 75) distribution in the tissues after subcutaneous introduction of SeO_2, the metabolism of selenium in tissues and its elimination after intratracheal introduction of SeO_2 as well as the distribution and the dynamics of elimination after subcutaneous introduction of red amorphous selenium.

"The author stated that after subcutaneous introduction of SeO_2 during the period of 24 hours about 7.5 p. c. of the introduced dose is eliminated from the organism, especially in urine. Selenium metabolism is mainly a function of liver and the kidneys. After intratracheal introduction of selenium large fluctuations in the selenium content in different tissues were stated. In the case of high content of selenium in the lungs also a high content of it was found in the liver and a lower one in the kidneys. When the selenium content in the lungs was low, the relations were reversed.

"After the intratracheal introduction to rats of the red amorphous selenium the animals observed up to 3 months showed that the period of half-excretion of selenium lasted for 7 days. Moreover, the author stated that the scheme of selenium metabolism in the organism is the following: red cells, liver, plasma, kidneys, urine."

GALLAGHER, C. H. & SIMMONDS, R. A. **Prophylaxis of Poisoning by Carbon Tetrachloride.** [Correspondence.] *Nature.* 1959, Oct. 31, v. 184, Suppl. No. 18, 1407–8.

Experiments were undertaken to find whether the effects of CCl_4 poisoning in rats would be prevented by agents which stimulate the synthesis of pyridine nucleotides and increase their concentrations in the tissues. The agents were nicotinic acid and its precursor, tryptophan. They were effective to a degree which depended on the length of pretreatment. The rats weighed about 150 gm. Each day 50 mgm. of the agent was injected intraperitoneally. CCl_4 was administered intragastrically.

Mortality rates in controls given 0·6 or 0·4 ml. CCl_4 were 52/52 and 40/47. Nicotinic acid was given on the same day as 0·6 ml. CCl_4, or also on the day before or also on 2 days before. DL-tryptophan was given similarly before 0·4 ml. Mortality rates in 3 nicotinic acid groups were 16/18, 5/8 and 2/17 and in 3 tryptophan groups 6/8, 6/9 and 5/16. Even 1 day's pretreatment on the same day as the poison gave slight protection, but the effect of this timing was not improved by adding 50 mgm. glutathione to the nicotinic acid or by reducing the poisonous dose to 0·4 ml. or by combining tryptophan with nicotinic acid. Similar pretreatment with 200 mgm. methionine intragastrically or 50 mgm. glutathione or glucose intraperitoneally did not alter the animals' susceptibility, though the first 2 have been reported to be useful in therapy [this *Bulletin*, 1959, v. 34, 549].

Consideration of the biochemical basis of liver damage from CCl_4 makes it appear that in work with rat liver mitochondria CCl_4 promotes the loss of respiratory cofactors, thereby inactivating enzyme systems which required pyridine nucleotides. The authors suggest that their results support the idea that it is this loss which kills cells. Increased tissue concentrations of pyridine nucleotides presumably maintain higher mitochondrial coenzyme levels, so sustaining respiratory activity during the critical period of the maximal effect of CCl_4.

M. Patricia Fitzsimons

SHIRAKAWA, M., NAGATOSHI, H., HIRAKAWA, M., SATO, E., YAMASAKI, S. & KATSUYAMA, G. **Hygienic Investigation on Workers dealing with Pentachlorophenol (PCP) in a Rubber Manufacturing Industry.** *Kurume Med. J.* 1959, v. 6, No. 1, 24–35, 3 figs. [33 refs.]

Excretion estimations were among the investigations of a 3 months' clinical survey undertaken when some workers developed dermatoses 1 month after sodium pentachlorophenate (Na-PCP) was added to the rubber cement used in a factory in Kurume, Japan. The fingertips and distal part of the palms were affected, mainly among 2 groups of 12 and 10 women, aged 15–22, who brushed a 3·5% Na-PCP cement on cloth linings for rubber boots. Hyperkeratosis and rhagades, fingertip abrasions and disappearance of whorls were accompanied in some by tingling and numbness. Work did not cease, efforts were made to prevent contact and 2 months later the skin had almost recovered to a state which was similar to that of 22 controls, who did similar work using the cement without Na-PCP, some of whom, however, had fingertip smoothing and abrasions (and, according to one of the tables, hyperkeratosis in 4 control brushers). 2 girls who matched cloths pasted with Na-PCP cement by machine and 4 men, aged 38–47, who mixed the cement, and their 6 controls were apparently unaffected.

The monthly survey of these 56 people consisted of testing the weight, tendon reflexes, sensation and blood pressure, of measuring the blood count, sedimentation rate and blood sugar and of quantitative urinary analyses for urobilinogen, protein, sugar, sediment and PCP. Mean results for each pair of groups are compared and discussed. Abnormal findings were slight in degree: increased blood sugar, decreased blood pressure and more frequent positive urobilinogen tests in the Na-PCP groups. Among exposed and controls slight anaemia developed and the red blood cells in the urinary sediment increased during the survey. That absorption of PCP took place, without producing characteristic symptoms of poisoning, is shown by urinary PCP values in monthly random samples from 7 brushers which averaged 2·6 and 2·8 mgm. per litre, controls averaging 0·7 and 0·3; from 2 mixers the average was 0·4 mgm. per litre and their controls nil.

M. Patricia Fitzsimons

CORNISH, H. H. & BLOCK, W. D. **The Toxicology of Uncured Epoxy Resins and Amine Curing Agents.** *Arch. Indust. Health.* Chicago. 1959, Nov., v. 20, No. 5, 390–98, 2 figs. [15 refs.]

This comparative study deals with range-finding toxicity tests of a typical uncured epoxy resin, 2 uncured epoxy resin modifiers and 6 room-temperature amine curing agents (hardeners), 1 of which was experimental and of low toxicity. With the most toxic hardener acute and chronic inhalation studies were also carried out. Some structural formulae and the chemical and physical properties of the 9 compounds are indicated.

In rats, the single-dose oral toxicity and the 24-hour skin absorption test, given as the 14-day LD50, show the resin, which is of low toxicity and high molecular weight, to be less toxic than the low molecular weight modifiers. Rats survived an 8-hour exposure at room temperature to the concentrated vapour from 8 compounds, the exception being the volatile modifier. In rabbits the 24-hour skin irritation test produced only slight irritation except from the modifiers and 1 hardener; the corneal injury test, estimated after 24 hours, produced slight to moderate injury except from this irritative hardener. By range-finding techniques the resin was the least toxic; the modifiers and 5 hardeners had low to moderate toxicity. The irritative hardener was the most toxic by all routes except room-temperature inhalation.

In the chronic inhalation experiment, rats withstood exposure for 7 hours a day on 5 days a week for 4 months to this agent, vapourized at 50°C., in a concentration of 0·0198 mgm. per litre; no injury was detected, based on mortality, growth, tissue pathology, organ enlargement, urinalysis or blood changes. The acute inhalation experiments included 2 at 100°C. to achieve a concentration of 0·134 mgm. per litre (0·00246 mEq. of amine nitrogen per litre); this produced mortality ratios of 9/14 and 32/36, some haemoconcentration and slight liver change.

M. Patricia Fitzsimons

STEFFEE, C. H. **Histopathologic Effects of Rare Earths administered intraperitoneally to Rats.** A Preliminary Report. *Arch. Indust. Health.* Chicago. 1959, Nov., v. 20, No. 5, 414–19, 5 figs.

Stable isotopes of rare-earth compounds were used in these experiments after trials with radioisotopic forms in malignant peritoneal or pleural effusions, and as a result of the granulomatous inflammation produced in the animals the autopsy material of the patients was reviewed. [See also this *Bulletin*, 1950, v. 25, 1268; 1958, v. 33, 485; *Federation Proc.*, Wash., 1957, v. 16, 207; CRESS and KYKER, *Problems in the Establishment of a Colony of Specific Pathogen-Free Rats.* 1957, U.S. Atomic Energy Report, ORINS,-22.]

Rats were injected intraperitoneally with cerium, lanthanum, yttrium, praseodymium, neodymium or the mixture of rare earths, C-340. Each was given as the chloride, 60 mgm. per ml., in doses of 25, 50, 100 or 200 mgm./kgm. Controls were given NaCl solution but in future will be given acid solutions. Some animals died as a result of rare-earth toxicity, or epidemic pneumonitis, or both. The remainder were killed 22–117 days after injection and none showed clinical effects.

Shortly after injection many animals developed severe ascites, perhaps due partially to the acidity of the solutions; some succumbed and had up to 200 ml. of ascitic fluid; survivors reabsorbed this fluid. Subsequently the acute inflammatory fibro-purulent reaction developed into granulomatous peritonitis on all surfaces including the liver capsule; discrete granulomata had occasional multinucleated giant cells. This is illustrated by photographs. Focal hepatic necrosis appeared in 11 of 117 animals, early after the large doses, but not after neodymium. Tables give doses, survival periods and amounts of ascitic fluid or severity of

hepatic necrosis. Changes in myocardium, kidneys and adrenals were incidental to the epidemic.

Another table gives data of 18 patients who had been given radioactive yttrium or lutecium intravenously or intraperitoneally. There was no evidence of granulomatous peritonitis, but the doses were smaller. A few patients had peritonitis which may or may not have been due to isotope administration since they had widespread carcinomatosis. One had a fatty liver and hepatic necrosis, probably due to purulent peritonitis but possibly to added damage from the rare earth.

M. Patricia Fitzsimons

HAAGEN-SMIT, A. J., BRUNELLE, M. F. & HARA J. **Nitrogen Oxide Content of Smokes from Different Types of Tobacco.** *Arch. Indust. Health.* Chicago. 1959, Nov., v. 20, No. 5, 399–400.

Mechanical smoking procedures are described in 2 comparative surveys. In the first, about 400 ml. of smoke was delivered at "normal" smoking rates, *i.e.* allowing 6–10 minutes for smoking a cigarette. 21 brands were tested and there was no significant difference in the concentrations of oxides of nitrogen from ordinary size cigarettes or large, *i.e.* king-size, whether with or without filter tips. A table sets forth the burning times, residual length of tobacco, gas volumes delivered, percentages of CO_2 and concentrations of NO plus NO_2 (NOx). The CO_2 varied from 7% to 11·4% and the NOx from 145 p.p.m. to 655 p.p.m. (V/V). The NOx from 5 brands of cigars varied in 7 tests from 167 p.p.m. to 1,250 p.p.m., and from 2 pipe mixtures was 125, 403 and 1,154 p.p.m.

In the second experiment the effect of burning rates was tested in similar king-size cigarettes. 660 ml. of smoke were produced under continuous suction of 4 ft. of water differential pressure or under ½ inch suction, in 30 seconds from 1¼ inch and in 7½ minutes from 3 inches of cigarette respectively. The fast burning produced 400 p.p.m. of NOx and 6% CO_2; the slow burning produced 136 p.p.m. and 3·2%.

When smoke was inhaled, no oxides of nitrogen were detected in the exhaled smoke; if it was not inhaled into the lungs, the NOx content of the exhaled smoke was approximately one-third of the original concentration. When investigating the effects of smoking on health, the oxides of nitrogen should be taken into account.

M. Patricia Fitzsimons

GRZEGORCZYK, L. & MAZUROWA, Janina. W sprawie szkodliwego działania furfurolu. **[The Toxic Action of Furfurol (Preliminary Report)]** *Med. Pracy.* 1959, v. 10, No. 3, 199–202.

The English summary appended to the paper is as follows:—

"The authors have carried out the medical and environmental examinations in the petrol refinery, where furfurol was used for refining purposes. The furfurol content in the air was many times greater than maximum allowable concentration. In the employees exposed to hazard the disturbance of the nervous system as well as the dermatologic changes in form of eczema, dryness, defective keratosis of epidermis and overpigmentation of the skin were stated.

"The results of these examinations show that in the conditions of furfurol hazard the rules of occupational hygiene must be observed exactly."

SANDERSON, D. M. & EDSON, E. F. **Oxime Therapy in Poisoning by Six Organophosphorus Insecticides in the Rat.** *J. Pharmacy & Pharmacol.* London. 1959, Dec., v. 11, No. 12, 721–8. [33 refs.]

The rationale of oxime therapy in poisoning by organophosphate compounds is outlined.

The effect was assessed of 2 oximes, pyridine-2-aldoxime methiodide (P2-AM) and bis (pyridine-4-aldoxime) trimethylene dibromide (TMB4) on rats poisoned by a number of organophosphate compounds used commercially as insecticides. In some cases blood and brain cholinesterase levels in treated and untreated rats were compared.

P2-AM 100 mgm./kgm. and TMB4 25 mgm./kgm. were given intraperitoneally 15 minutes before and 4 hours after and subcutaneously 8 hours after the insecticide which was given orally. The LD50 of the insecticides was also determined. P2-AM and TMB4 reduced the mortality after poisoning by parathion and parathion methyl, diazinon and phenkaptone. They had no effect on dimethoate (*OO*-dimethyl-*N*-methylcarbamoylmethyl phosphorodithioate) or dimefox. P2-AM did not enhance the therapeutic value of atropine in rats poisoned with dimethoate. There was little difference in the efficacy of the two oximes. TMB4 is much more soluble than P2-AM.

J. M. Barnes

BECKER, S. W. & O'BRIEN, M. P. **Value of Patch Tests in Dermatology. Special Study of Follicular Reactions.** *Arch. Dermat.* 1959, May, v. 79, No. 5, 569–77, 9 figs. [18 refs.]

After partial recovery from extensive autosensitization dermatitis 110 patients were tested with a series of 24 chemicals. 56 similar patients were tested against 14 oleoresins.

In 69 patients eczematous or follicular reactions were given against the chemicals, while 16 patients gave erythematous, oedematous, and sometimes vesicular reactions to the oleoresins. Serial biopsies on patients with follicular reactions showed the primary reaction to be dermal, the folliculoporal epidermal vesiculation being a secondary phenomenon. Positive follicular reactions suggested dermal allergy, the primary dermatitis being possibly constitutional in nature. Where all tests were negative it was suggested that the primary dermatitis was also constitutional. Recurrent dermatitis after removal of contact with chromates may also be constitutional in nature.

H. T. H. Wilson

OCCUPATIONAL PSYCHOLOGY

World Health Organization. Technical Report Ser. No. 183. **Mental Health Problems of Automation. Report of a Study Group.** Geneva, 10–15 November 1958. 30 pp. 1959. Geneva: Palais des Nations. [Sales agent for U.K.: H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

The word "automation" has no one accepted definition. This report accepts the British definition of the Department of Scientific and Industrial Research: "The coming together of several relatively independent streams of technical progress".

As a rule this includes 3 relatively distinct fields; "Detroit automation" which is a highly developed mechanization; "control automation", the control of machines by machines; and "computer automation", the development of the electronic digital computer. Of these the third is the most revolutionary in that it is introducing changes into office work which hitherto has been little affected by mechanization.

Views as to the impact of automation vary greatly, from those of extreme optimism in its potential economic benefit to those of extreme pessimism on account of the social and psychological implications. In terms of mental health the new developments must be recognized as having implications at least as important as those of the Industrial Revolution. Although some automation (*e.g.* the telephone exchange) has already taken place without arousing much public attention, the new office developments may be expected to have a more noticeable impact on the public. The life of the individual is built around a variety of social groups—the family group, the work group, and so on. Though worsening of conditions in one such group may be compensated by improved relations elsewhere, it is still necessary to examine the changes that affect the worker either as a member of a work group or as an individual. The threat of change may produce emotional reactions no less real than actual change, and ignorance about the nature of an anticipated change may bring about wholly erroneous beliefs which have no basis in reality. There are a variety of techniques which have been employed by different organizations to prepare the way for change. To achieve this successfully, "it is urgent for managers and engineers to have at least some basic knowledge of the social and behavioural sciences".

It is also necessary to consider the situation brought about by the actual changes, as distinct from the anticipation of change.

There are a number of ways in which the development of automation will inevitably bring about changes; for example, perceptual work gradually replaces manual work, subliminal attention may be required, and long periods of vigilance may lead to nervous strain. At the same time individuals may become remote from their workmates and their supervisors, and to some extent even more remote from their machine. As the consequences of making an error become greater so the machine operator's feelings of responsibility tend to increase, resulting in further mental strain.

These are all potential sources of extra strain and all require preventive attention. Such attention needs to be directed towards the techniques of selection, training, changes in work, opportunities for relaxation, and machine and equipment design.

A new relationship between factory worker and office worker may have advantages for the former in up-grading factory morale, but may have disadvantages for the office worker in producing status problems. Possible new patterns of living will require collaboration between architects and planners and mental health workers.

There is need for much more research into the adaptation of the individual, the family and the community to automation. *H. G. Maule*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

Buttiaux, R. **The Value of the Association Escherichieae-Group D Streptococci in the Diagnosis of Contamination in Foods.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 153–8, 1 pl. [20 refs.]

The use of *Escherichia coli* as an indicator species for faecal contamination of foodstuffs should be reconsidered for the following reasons: The proportion of *Klebsiella* in human faeces in one series rose from 5·2% in 1947 to 48·4% in 1956–57; *E. coli* and other *coli-aerogenes* organisms may be absent from the gut of certain animals, notably the pig; usual methods of counting coliform organisms do not include those strains fermenting lactose slowly or not at all; these occur in 35·6% of human faeces and methods of detecting such strains may be unsatisfactory; the origin of the *coli-aerogenes* group of bacteria is uncertain. Considering other organisms, *Clostridium welchii* may come from faeces or from soil; many foods contain soil strains only. It is suggested that Group D streptococci including *Str. faecalis* var. *zymogenes* and *liquefaciens, Str. faecium, Str. durans, Str. bovis,* and *Str.*

equinus are better indicators of faecal contamination. They are consistently and frequently found in the intestine of man and animals, often in greater numbers than *coli-aerogenes* bacteria, and may be readily isolated with modern selective media and membrane filter techniques [this *Bulletin*, 1958, v. 33, 495]; when found in association with *coli-aerogenes* bacteria a diagnosis of faecal contamination in foodstuffs is said to be justified.

With *E. coli* as the test organism, pollution was detected in 92·4% of waters, from 106 catchment areas; with group D streptococci the figure was 90·5%; *Cl. welchii* was detected in 74·5% only of polluted waters. Most faecal streptococci, except *Str. bovis* survive better than *coli-aerogenes* bacteria in water or other natural media, and also in products which have inhibitory properties for the coliform group, *e.g.*, citrus juices [*ibid.*, 1956, v. 31, 659], frozen foods [*ibid.*, 1958, v. 33, 968] and meat brines [*ibid.*, 1959, v. 34, 70]. *Betty C. Hobbs*

THOMAS, S. B., HOBSON, Phyllis M. & DRUCE, R. G. *Coli-aerogenes* **Bacteria in Farm Water Supplies.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 32–45. [28 refs.]

Samples of untreated water supplies intended for dairy purposes on farms in Wales were taken from springs arising above and some distance from farmsteads, wells situated near the dairy or farmhouse and from surface water liable to pollution from sheep and cattle; local authority chlorinated water was not included. Samples were also taken at fortnightly intervals for 12 months from 11 farm water supplies to determine seasonal variation in the incidence of different types of *coli-aerogenes* organisms; the sources included 7 springs, 2 wells, and 2 upland streams. The waters were examined within 6 hours of sampling. Quintuplicate 10, 1 and 10^{-1} amounts of water were inoculated into MacConkey broth and incubated for 5 days at 30°C., and similar quintuplicate sets were incubated for 2 days at 37°C. Tubes positive at 37°C. were subcultured at 44°C. for 2 days to determine the presumptive count of *Escherichia coli* I.

The highest positive dilutions at 37°C. and at 30°C. were plated on to Difco eosin methylene blue agar to obtain colonies for differential tests. 825 cultures of *coli-aerogenes* bacteria were isolated at 30°C. and 735 at 37°C. from 645 samples of farm water supplies which were classified according to the recommendations of the Coliform Sub-Committee of the Society of Applied Bacteriology, Report 1949 [this *Bulletin*, 1950, v. 25, 1065]. 50% of cultures isolated at 30°C. were *Klebsiella* and 57% of cultures isolated at 37°C. were *E. coli* I. It is suggested, therefore, that incubation at 30°C. is as selective for *Klebsiella* as 37°C. is for *Escherichia*. *Citrobacter freundii* I and *K. cloacae* were found predominantly in waters of high sanitary quality from protected springs and wells; the microflora of polluted water was dominated by *E. coli* I, isolated from 43% of samples incubated at 30°C. and from 76% of those incubated at 37°C.

There was a marked seasonal variation in the incidence of the different types isolated at 30°C.; there was a higher proportion of *E. coli* I in summer than in winter, while *Klebsiella* and *Citrobacter* showed a higher proportion in winter than in summer. The authors suggest that further information is required on the serological classification of *E. coli* I cultures derived from polluted waters, according to the antigenic scheme established by KAUFFMANN [*ibid.*, 1955, v. 30, 1036]. *Betty C. Hobbs*

GRIFFITHS, D. G. & THOMAS, S. B. **The Bacterial Content of Farm Dairy Equipment.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 46–51.

2,310 rinse samples from dairy equipment on 750 farms were examined during 1956–1957 at fourteen Ministry of Agriculture laboratories in Wales. Samples were examined within 4 hours of collection; to each rinse of 500 ml. of quarter-strength Ringer solution, sodium thiosulphate was added for equipment treated with hypochlorite, and lecithin-Lubrol-W solution for equipment cleansed with quaternary ammonium compounds. Colony counts were made in Yeastrel milk agar incubated for 3 days at 30°C. *Coli-aerogenes* tests were made in 3 tubes of MacConkey broth inoculated with 1 ml. of rinse and incubated for 3 days at 30°C. For milk spoilage organisms 1 ml. of rinse was inoculated into 5 ml. of sterile litmus milk and incubated at 22°C. for 2 and 3 days.

Rinses from milking machine clusters gave more unsatisfactory results than those from metal equipment. Results from clusters sterilized with steam were much better than those from clusters claimed to have been cleansed by chemical methods. 76% of rinses from milking machine clusters sterilized by steam had colony counts less than 10^4 per sq. ft., and 8% only had counts exceeding 5×10^4 per sq. ft. A high proportion of advisory rinses from clusters exceed this level, indicating that non-sterile dairy equipment is common on farms where milk has been rejected or failed the statutory test; clusters containing more than 2·5 million viable organisms, including *coli-aerogenes* and active milk spoilage organisms, were considered to be grossly contaminated.

The authors suggest that comparative results obtained for equipment sterilized by steam and the various chemical methods should not be interpreted as an indication of their respective merits; for the majority were obtained at farms where milk of poor keeping quality had recently been reported, and it was rare to find that approved methods of chemical sterilization had been followed. It has previously been reported that for sterilization hypochlorite is not inferior to steam or boiling water. *Betty C. Hobbs*

DONOVAN, Kathleen O. **The Occurrence of *Bacillus cereus* in Milk and on Dairy Equipment.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 131–7. [14 refs.]

In an investigation of 2 large Scottish creameries pasteurizing milk received in cans from individual farms and in road tankers from collecting depots, samples were

taken from different parts of the plant, road tankers and the weight tank, also from farms and collecting depots; samples were refrigerated until examined. Part of each sample was pasteurized at 63°C. for 30 minutes; pour plates with egg yolk inhibitor agar were made with raw milk samples and rinse and swab suspensions, and plain egg yolk agar was used for the pasteurized samples, all incubated at 30°C. for 18 hours. Vegetative cells were obtained from cultures in glucose peptone water at 22°C. and the absence of spores was confirmed by plate counts after heating for 30 minutes at 65°C. Results showed that 87% of milk samples contained fewer than one cell of *Bacillus cereus* per ml., the remaining 13% gave low counts and indicated that *B. cereus* occurred in milk received from particular farms and creameries. The source of contamination was mainly empty cans allowed to stand a long time before being washed properly and 'sterilized'. Vegetative cells of *B. cereus* formed spores readily in the thin film of diluted milk in rinsed cans. It is suggested that except for milk cans the organism rarely spores on dairy equipment; the same factors may apply to imperfectly cleaned milk bottles, from which pasteurized milk could be contaminated.

Betty C. Hobbs

MURRAY, J. G. & COEY, W. E. **The Effect of Freezing and Storage on the Bacterial Flora of Pasteurized Milk.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 125–30.

Samples of pasteurized milk (High Temperature Short Time) were taken throughout the year. 1 pint quantities in polythene bags were immersed in brine at − 28°C. for 60–65 minutes and stored at − 12° for 6 months. Comparisons before and after freezing were made by colony counts on yeastral milk agar at 3°, 22°, 30°, and 37°C., after 21, 5, 3 and 2 days' incubation respectively, and by plating 1 ml. of undiluted milk and 1/10 dilutions on violet red bile agar incubated at 30°C. for 18–24 hours for coliform counts. The flora before and after freezing was compared at 30°C. and 1 ml. quantities were examined for *Pseudomonas fluorescens*. There were significant changes in counts after storage for 4–5 months at − 12°, coincidental with physical changes. The milk remained normal for 6 weeks; up to 17 weeks it could be reconstituted by boiling and shaking, but not after 18 weeks; the acidity was unchanged. The normal flora was unaltered by freezing and limited storage, and when coliform organisms were added as contaminants the numbers were not decreased by freezing.

Samples taken on different days reacted differently to freezing and storage. *Betty C. Hobbs*

MOCQUOT, G. & BÉJAMBES, Marie. **Bacteriology of Goats' Milk and Ewes' Milk and their Products.** *Dairy Sci. Abstracts.* 1959, Dec., v. 21, No. 12, 531–7. [Numerous refs.]

The review covers the natural bacterial content of both goats' and ewes' milk sampled aseptically, and also on delivery after normal milking procedure; references are given to the bacteriology of milk produced from animals suffering from mastitis, brucellosis, Q fever, tuberculosis, and miscellaneous infections such as meningo-encephalitis, salmonellosis and contagious agalactia. Reports of mastitis caused by streptococci, staphylococci, *Clostridium welchii*, *Escherichia coli*, *Bacterium putidum* and *Nocardia asteroides* are given for goats, and organisms of the intermediate coliform group, *B. tertius*, *Staph. aureus*, *Staph. albus*, *Past. mastitidis*, *Corynebacterium pyogenes and Histophilus ovis* are reported as causing mastitis in the ewe. Methods of treatment by vaccines and antibiotics are quoted. References are given to methods for the rapid detection of brucellosis by examination of milk with the ring test or by whey agglutination and also by bacteriological examination. References to reported cases of infection, experimental infection and the beneficial influence of pasteurization are quoted.

Evidence for the transmission of Q fever to man through milk is given and also the effect of pasteurization on *Rickettsia burneti* in milk.

References are given also to tuberculosis in goats.

Betty C. Hobbs

FOOD POISONING

DIXON, W. M. & GARDNER, A. W. **An Outbreak of Staphylococcal Food Poisoning at Esso Refinery, Fawley.** *Med. Officer.* 1959, Oct. 9, v. 102, No. 15, 181–3. [14 refs.]

5 persons out of approximately 210 at risk were acutely ill with vomiting, diarrhoea and abdominal pain, 2 to 3½ hours after a meal in which 1 of 14 trays of milk pudding, each intended for 15 persons, was the only common food. Coagulase-positive staphylococci, phage type 6/42/47/53 + (Group III) resistant to penicillin but sensitive to chloramphenicol, erythromycin, streptomycin and tetracycline, were isolated from a sample of rice pudding taken from the dustbin, from the stools and vomit of 1 patient; from the hands of 2 cooks, and from the nose of one waitress. Rice, sugar, and dried milk were used for the milk puddings said to be prepared and cooked within 3½ hours of the meal. The origin of the staphylococcal enterotoxin is discussed. *Betty C. Hobbs*

STOKES, R. *Salmonella* **Food Poisoning traced to Duck Eggs.** *Irish J. Med. Sci.* 1959, Nov., 6th Ser., No. 407, 481–500. [Numerous refs.] Discussion 500–501.

2 ducks eggs eaten fried were suspected to be the vehicle of *Salmonella typhi-murium* infection in 1

patient. Sera from 8 of the 13 ducks concerned gave significant H titres against *Salm. typhi-murium*. 11 of the ducks were kept under observation for 12 months. Faeces were negative; 82 eggs were examined and 2 positive yolks were found after 8 months. Post-mortem examination of 7 remaining birds showed one spleen only positive for *Salm. typhi-murium*, but all the birds showed evidence of tuberculosis. It was assumed that one or more of the 13 ducks were chronic carriers of *Salm. typhi-murium* and were producing contaminated eggs. It is suggested that the ducks were infected by consuming rodent faeces or urine or both with their feed, although the examination of rats on the farm gave negative results.

The author discusses references to infected rats, proportion of infected eggs from carrier birds, numbers of organisms in the eggs in relation to an infectious dose, effect of cooking, and the value of blood testing in identifying infected birds and its relationship to ovarian activity. The discussion broadened to give a general survey of food-poisoning due to salmonella infection. Reports on incidence and proved sources, such as the human carrier, poultry, eggs and egg products, pigs and pork products, cattle, rodents, domestic pets (cats and dogs), organic fertilizers, and animal feeding stuffs are quoted. Examples of outbreaks are given and a special section is devoted to food-poisoning in Eire.

Betty C. Hobbs

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

CHMEL, L. **Critical Survey of Medical Mycology in Czechoslovakia for the Years 1946 to 1956.** *Mycopathologia.* The Hague. 1959, Dec. 30, v. 12, No. 1, 77–95, 2 figs. & 3 graphs. [92 refs.]

HADIDA, E. & SCHOUSBOE, A. Aspects de la maladie dermatophytique. [**Aspects of "Dermatophytic Disease"**] *Algérie Méd.* 1959, Apr., v. 63, No. 4, 303–36, 46 figs. [80 refs.]

This is a review of 7 cases of dermatophytosis, most of which have already been recorded in the literature by these authors. Their purpose in publishing this article is to challenge the traditional and almost universally established belief that the parasitic activity of dermatophytes in human beings and animals is confined entirely to the keratin-containing tissues which comprise the stratum corneum, the hair shaft and the nails.

In all the cases reviewed, except one, a generalized cutaneous eruption was present associated with an intense pruritus.

3 were cases of generalized favus attributed to *Trichophyton schönleini* (syn. *Achorion schönleini*) while the infection in the other 4 patients was attributed to *T. verrucosum*. Scutula were present in only 1 of the patients suffering from favus, the other 2 exhibiting lesions which were trichophytoid in character. Total alopecia which involved the eyebrows was associated also with the favus in the scutulum-bearing patient, whereas the other 2 favic patients suffered scarcely any loss of hair. All the patients presented with onychomycosis in addition to lesions in other parts of the body.

In 3 of the patients suffering from *T. verrucosum* infection the external auditory meatus was invaded by the fungal parasite.

In 5 patients intradermal granulomata were observed in biopsies obtained from them, but in only 2 cases were they seen to be centred around keratinous material.

In the 3 patients suffering from favus the superficial lesions were crusty, ulcerated or vegetating, and were deep-seated, penetrating to the aponeurosis. Lesions were found even in bone.

3 of the patients (those with generalized favus) died in a cachectic state.

At autopsy, it was found that, in these patients, there was a deep-seated adenitis as well as visceral lesions which varied in character and distribution according to the case; extensive perivisceral inflammation, especially of the liver, pericarditis, brain lesions, lesions in the thymus; and lastly, in all cases, fatty degeneration of the liver.

Mycelium attributed to the fungi already named was demonstrated histologically in the mediastinal glands, spleen and liver, and in fragments of necrosed bone in one case; in the cerebral cortex, lymphatic glands (in the vicinity of the internal iliac artery), in the liver and in the spleen, in another; and in the third case, in the mediastinal and mesenteric glands as well as in the liver.

It was concluded from the results of animal inoculation with ground up hepatic nodules obtained from 2 of these fatal cases, that the tubercle bacillus was present in these lesions in which mycelium (attributed to the above-mentioned dermatophytes) was also demonstrated histologically.

In regard to the 4 surviving patients, the authors were satisfied that the pus from deep-seated suppurative

intradermal lesions contained abundant mycelial elements as was also the case with pus obtained from suppurating regional lymphatic glands. From clinical and laboratory investigations they also concluded that organic disease of mycotic origin (dermatophytes) was present in these patients.

[In support of their claims the authors quote numerous cases of deep-seated mycosis in the literature which were attributed likewise to dermatophytes by other investigators.] *C. J. La Touche*

SCHWARZ, J. **Incidence of Dermatophytes in Cincinnati and Some Diagnostic Laboratory Procedures.** *Arch. Dermat.* 1959, Nov., v. 80, No. 5, 538–42, 2 figs.

In Cincinnati General Hospital the dermatophyte most frequently isolated during the period 1950–1958 was *Microsporum audouini* (1,363 times).

Usually there was no difficulty in identifying this species in culture and in cases of doubt, its characteristic growth on rice grains decided the issue.

M. canis, traced usually to infected kittens in the affected family, was isolated much less frequently (43 times), and *M. gypseum* even less frequently (9 times).

A comparative survey of the incidence of dermatophytes in approximately the same number of wild and domesticated animals showed that in wild animals the incidence was only 0·51% of the total incidence whereas it was 27·2% in domesticated animals (chiefly cats and dogs infected by *M. canis*). This is shown in tables adapted from KAPLAN *et al.* (*Ann. New York Acad. Sci.*, 1958, v. 70, 636).

In the case of the anthropophyllic species *Trichophyton rubrum* and *T. mentagrophytes*, some strains which were difficult to identify on standard Sabouraud media were identified by means of the sterile hair test [this *Bulletin*, 1957, v. 32, 706] which shows that *T. mentagrophytes* forms penetrating organs which attack the hair, whereas *T. rubrum* is unable to do so. It was also found that griseofulvin used *in vitro* enabled one to distinguish between these two species as it markedly inhibited the growth of *T. rubrum* whereas it was much less fungistatic for *T. mentagrophytes.*

In the case of species such as *T. tonsurans* (isolated 48 times) which comprises a variety of cultural types, morphological identification could be confirmed by studying the nutritional pattern as recommended by GEORG and CAMP [*ibid.*, 1958, v. 33, 282] who showed that strains of *T. tonsurans* were stimulated by thiamine when they were grown on a basal medium to which thiamine was added, whereas strains of *T. mentagrophytes* and *T. rubrum* which sometimes superficially resembled *T. tonsurans* were not stimulated by the addition of this vitamin to the culture medium. *C. J. La Touche*

ZAMIECHOWSKA-MIAZGOWA, J. **Chemical and Antigen Structure of** *Trichophyton sulphureum. Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 11, 445–9.

GRIN, E. I. Nova terapija dermatofitija vlasišta oralnom upotrebom griseofulvina i mehanizam njegovog djelovanja. [**New Therapy for Ringworm of the Scalp by Oral Administration of Griseofulvin. Its mode of Action**] Reprinted from *Vojnosanitetski Pregled.* 1959, v. 10, 771–80, 10 figs. [13 refs.] English summary.

The author treated 39 patients with ringworm, finding that oral administration of 1 gm. griseofulvin twice each week for adults (and correspondingly less for children) was effective in producing complete cure in 3–5 weeks. The infections were due to *Trichophyton violaceum* and *T. schoenleini.* There were no side effects.

It was desirable, however, to remove the hair at the beginning of treatment and again after 3 weeks, so as to avoid reinfection from any reservoir of parasites remaining on the scalp. It was also desirable to wash the head every second day and to use fungicides on materials which could harbour viable fungi.

Inflammatory forms of dematophyte infections of the scalp (kerion), mostly caused by zoophilic species, did not respond to griseofulvin, but on the contrary the inflammatory reactions of the lesions were exacerbated in infections with *T. verrucosum* and *T. mentagrophytes.*

The author discusses the mode of action of griseofulvin. *Charles Wilcocks*

MACLEOD, J. & NELSON, W. O. **Griseofulvin and Human Spermatogenesis.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 259–60.

"Daily administration of 2g of griseofulvin to 14 normal men for 3 months did not produce significant changes in semen quality or in histology of the testes of 8 of the individuals."

RIDLEY, M. F. & NOWELL, T. A. **Another Australian Case of Histoplasmosis.** *Med. J. Australia.* 1959, Oct. 31, v. 2, No. 18, 640–41, 3 figs. (2 on pl.) [10 refs.]

"An apparently transitory infection of the jaw of a Rockhampton man with *H. capsulatum* was diagnosed histologically, and confirmed by culture. The organisms were not recovered from samples of soil and sawdust from his garden and fowl yard. A histoplasmin survey of the district gave six weakly positive reactions in 768 persons tested."

i. VINCE, S. **The Spread of** *Candida* **in Infants and Children.** *Med. J. Australia.* 1959, Aug. 1, v. 2, No. 5, 143–5.

ii. ——. **Generalized Endogenous Mycosis in Childhood.** *Ibid.*, 145–9. [35 refs.]

i. "Five hundred infants and children in Budapest, Hungary, and 436 infants and children in Sydney were investigated for the presence of *Candida.*

"The percentages of positive findings in the new-born

and healthy children were in close agreement in both groups. The incidence of fungi in the children in hospital was twice as high in Budapest as in Sydney. The importance of hygienic conditions and nursing facilities is stressed.

"Blood and urine were investigated in a series of 60 infants who had received more than five days' broad-spectrum antibiotic treatment. Three infants yielded positive blood cultures; all of them were suffering from generalised candidiasis. From 19 infants, 30 positive urine cultures were obtained. In the majority of these, no clinical significance could be attributed to these findings.

"It seems that prolonged administration of antibiotics can influence the spread of the fungi within the body, and that it promotes their appearance in the urine. These findings in themselves probably do not signify a disease process. Positive blood cultures, on the other hand, seem to have always diagnostic significance."

ii. "A tabulated short history of nine children suffering from generalised endogenous mycosis has been presented.

"The problems of the diagnosis and pathogenesis of endogenous mycosis have been discussed in detail.

"A significant percentage of infants and children harbour yeast-like fungi on their mucous membranes, as was shown in the previous paper.

"It is considered that administration of antibiotics plays an important role in promoting the growth of fungi and can cause their spread within the body; but the decisive factor in the occurrence of secondary mycosis may be the lowering of the patient's resistance by lasting or recurrent infections.

"The need for complex therapy has been stressed."

GROSS, J. & RAUBITSCHEK, F. **The Action of Antibiotic S 68 on Moniliasis.** *Bull. Res. Counc. of Israel.* 1958, v. 7E, No. 4, 247–52.

No drug has so far been found which can satisfactorily halt the fatal progress of systemic moniliasis or systemic cryptococcosis in human subjects. The results of the therapeutic trials carried out with the drug used by the authors of this article should be therefore of special interest.

These trials were undertaken as a sequel to the discovery by RAUBITSCHEK [this *Bulletin*, 1957, v. 32, 506] of a water-soluble polyenic antibiotic S 68 derived from a soil streptomycete which was active *in vitro* against pathogenic yeast-like organisms such as species of *Candida* and *Cryptococcus*.

The authors decided to investigate the therapeutic activity of this drug in newly weaned mice in which systemic moniliasis had been induced experimentally with *C. albicans*.

In a first experiment, 30 mice were injected intraperitoneally with 300 million cells of *C. albicans*. Immediately after injection, 5 of these received 1,000 units of the drug intraperitoneally and 5 more received 500 units intraperitoneally. The remaining 20 did not receive any treatment.

All the untreated mice died within 18 hours, and *C. albicans* was recovered in culture from all the organs of these mice. During the next 2 weeks 2 of the mice which had received 1,000 units and 3 which had received 500 units of S 68 died. Autopsies of these mice showed numerous whitish nodules of pinhead size on the kidneys and on the spleens which were enlarged. Histological sections displayed granulomatous and abscess-like lesions in which were numerous fungal structures. The remainder of the treated animals made a complete recovery, and moreover, at 17 days after inoculation, showed a marked gain in weight.

In a second experiment, 4 mice injected intraperitoneally with 2·5 million cells of *C. albicans* remained unaffected at 7 days after injection and cultures made from them were sterile.

In a third experiment in which 31 mice were used, 16 received 60 million and 15 received 120 million cells of *C. albicans* intraperitoneally. Of the 16 mice which received 60 million cells 6 died within 48 hours of injection and the other 10 were acutely ill. Autopsy findings included nodular lesions in all the internal organs, and cultures from these organs were all positive except in the case of the brain. Of the 15 mice which had received 120 million cells, 13 died within 48 hours after injection and 2 survived. At autopsy, nodular lesions were observed in the liver and spleen, and cultures from all the internal organs including the brain, were positive. The 12 surviving mice were then treated on the third day after inoculation with 500 units of S 68 daily for 9 days administered subcutaneously. During this period 4 mice which had been inoculated with 60 million cells had died. All organs at autopsy showed white nodules of pinhead size. A few more died, and finally, 30 days after inoculation 5 of the mice which had received 60 million cells of *C. albicans* still survived. When these were killed and autopsied it was seen that one of them, a female, was pregnant, and showed no pathological changes in the viscera, while 3 had pale enlarged kidneys, and one of the kidneys in the fifth "was covered with abscesses". No local reaction was observed at the sites of the subcutaneous injections of the antibiotic.

In a final experiment in which 25 mice were used, the mice were inoculated with 25 million cells intraperitoneally. Later, 5 days after inoculation, by which time the disease had become well established, a subcutaneous injection of 100 units was administered to 8 of the mice and was continued daily for a total period of 10 days. 200 units were administered by subcutaneous route daily to 8 further mice for the same period. 5 weeks later all the mice were killed, and it was found that, whereas pathological changes had taken place in most of the internal organs in the untreated mice, those which had been treated did not show such changes, with the exception of one mouse; moreover, while cultures from the untreated mice were positive, those made from the treated mice were negative.

In conclusion, it appears from the results of these experiments, that recently weaned mice are highly susceptible to infection by *C. albicans*, and are therefore suitable experimental animals for use in the assay of drugs which might be of therapeutic value in the control of systemic moniliasis; and also that the polyenic

antibiotic S 68 used in the foregoing experiments is therapeutically active when administered subcutaneously in daily doses of 100 to 200 units for a prolonged period in the presence of this disease when it is well established in mice by experimental inoculation.

C. J. La Touche

MARTIN, W. J., NICHOLS, D. R., SVIEN, H. J. & ULRICH, J. A. **Cryptococcosis. Further Observations and Experiences with Amphotericin B.** *Arch. Intern. Med.* 1959, July, v. 104, No. 1, 4–14. [10 refs.]

Cryptococcosis is usually a chronic disease but it may be characterized by spontaneous remissions which make evaluation of therapy difficult. Although cures of localized pulmonary cryptococcosis by lobectomy have been reported [this *Bulletin*, 1956, v. 31, 402; 1958, v. 33, 347], the treatment of cryptococcal meningoencephalitis has been disheartening until the advent of Amphotericin B.

5 patients with the disease were given 50 to 100 mgm. of Amphotericin B dissolved in a minimum of 250 to 500 ml. of 5% dextrose in distilled water intravenously daily for approximately 6 weeks and in 3 the condition appeared to be arrested. In 2 patients, one of whom had associated Hodgkin's disease, relapse occurred.

It is not known whether intrathecal injection of the agent is necessary for the treatment of cryptococcal meningitis. Amphotericin B could not be detected in the cerebrospinal fluid of patients to whom it had been given intravenously and 3 were, therefore, given it by the intrathecal route. However, 1 patient apparently had clearance of the fungus from the central nervous system with only intravenous therapy and without showing detectable amounts of the antibiotic in the cerebrospinal fluid.

Phlebitis at the site of administration, headaches, flushing, chills, fever, dyspepsia and azotaemia may result from injections of Amphotericin B but prolonging the time of injection or decreasing or temporarily discontinuing the dose were effective in controlling these side effects and no permanent damage was observed.

Peter Abbott

BOJALIL, L. F., TRUJILLO, A. & CERBON, J. Diferenciación bioquímica de algunas especies de actinomycetes patógenos. **[Biochemical Differentiation of Various Species of Pathogenic Actinomycetes]** *Mycopathologia.* The Hague. 1959, Nov. 30, v. 11, No. 4, 287–96. [24 refs.]

The English summary appended to the paper is as follows:—

"In this paper a study is presented of the various properties of *N. asteroides, N. brasiliensis* and some pathogenic *Streptomyces*.

"The following aspects were studied: a) microscopic morphology, b) decomposition of several substances such as casein and tyrosine, c) gelatin hydrolysis and milk coagulation, d) acid production using different carbohydrate.

"From the results obtained it is deduced that two main groups exist within the genus *Nocardia*:

"Group I. Characterized by their ability to utilize casein and tyrosine, hydrolyse gelatin, coagulate milk and usually producing acid from inositol, galactose, glucose and fructose: only *Nocardia brasiliensis* belongs to this group.

"Group II. Microorganisms characterized by their low activity, inability to decompose casein and tyrosine, exceptionally they hydrolyse gelatin or coagulate milk. In this group we include all the strains received as *N. asteroides* and others such as *N. leishmanii, N. gypsoides, N. transvalensis, N. convoluta, N. polychromogenes, N. globerula, N. blackwellii, N. minima, N. pasteuroides, N. phenotolerans, N. corneus* and *N. melanosporus*.

"On the other hand *N. pretoriana, N. rhodnii* and *N. corallina*, have in common with *N. asteroides* the inability to utilize casein or coagulate milk, however, these strains decompose tyrosine, a characteristic which is not present in any other strains classified as *N. asteroides*, therefore it is necessary to carry out additional studies so that the taxonomic position of these "species" may be decided.

"The biochemical properties of *Streptomyces* were similar to those of *N. brasiliensis*, therefore it is not possible, through these methods, to make the separation of the genus *Streptomyces* from *N. brasiliensis*; the absence of fragmentation, the acid fastness and production of spores are the only differential characteristics that could be observed."

PEPYS, J., RIDDELL, R. W., CITRON, K. M., CLAYTON, Y. M. & SHORT, E. I. **Clinical and Immunologic Significance of *Aspergillus Fumigatus* in the Sputum.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 167–80, 2 figs. [16 refs.]

This article is a very full and informative exposition of the findings in an extensive investigation of the allergic and serological responses of 27 patients among 2,080 who attended the Brompton Hospital, London, with various chest disorders. It merits detailed study.

27 patients, of whom 23 were asthmatic, were investigated by direct bronchial sensitivity tests. 16 gave a positive bronchial reaction to *Aspergillus* extract while 11 did not react in this manner.

In 8 of the 16 patients who gave a positive bronchial reaction there was a family history of allergy; in 14 there were asthmatic symptoms as well, and in 7 others other allergic disorders were also present.

In 13 of the 16 patients X-rays revealed transient pulmonary shadows. Most of these had the appearance of consolidation-collapse and were usually segmental. In the majority of cases such signs were accompanied by febrile episodes although symptoms were not apparent. A high eosinophilia was present in the sputum of these patients (more than 500 eosinophils per cmm. in some). Tenacious plugs were expectorated by 6 patients, usually during febrile episodes, and contained eosinophils, debris and fungal elements.

The remaining 11 patients who did not exhibit any bronchial reactions to *Aspergillus* extracts, experience pyrexial episodes, show lung shadows on X-ray or produce sputum plugs nevertheless resembled the previous group of 16 patients in other respects, such as the frequency of a family history of allergy, a personal

istory of asthma and the presence of eosinophilia in ne sputum.

In 4 of the patients mycetomata were found in the ungs. In 2 or these the fungus grew in a preformed ir space: one in a pyogenic lung abscess and the ther in an apical air cyst. In a third it was present a segment with a partially narrowed bronchus. The formation of mycetomata seemed to depend pon the existence of previous bronchopulmonary isease and did not appear to be related to hyper-ensitivity to *Aspergillus*." One of these patients had long history of asthma, showed bronchial hyper-ensitivity to *Aspergillus* extracts, had eosinophilia in ne sputum, and transient shadows and febrile episodes, hereas the other 2 patients were not asthmatic, did ot have pulmonary eosinophilia and did not react to *spergillus* extracts.

In 8 patients X-ray opacity of the nasal antra was emonstrated and in 2 of these *A. fumigatus* was re-overed from wash-outs.

Various immunological tests were carried out, includ-ng skin tests in man, serological tests with rabbit ntisera, electrophoretic investigation of antigenic and llergenic components of *A. fumigatus* and serological ests with human sera and *Aspergillus* extracts.

Results of these tests showed that, of 27 patients ith *A. fumigatus* in the sputum, 16 were hyper-ensitive to bronchial and skin tests, and had episodes f pulmonary eosinophilia. The results of skin tests ith 1-month-old *Aspergillus* culture filtrates showed at patients who reacted to *Aspergillus* extract reacted o extracts from a number of other species of *Asper-illus* besides *A. fumigatus*. In addition to the mmediate weal reaction a delayed Arthus-type reaction as noted in some of these patients.

Precipitating bodies to *A. fumigatus* antigens were emonstrated, by means of the agar-gel diffusion test, n the serum of 13 patients in whose sputum *A. fumi-atus* had been found. This test was positive in the ase of 2 patients who did not react either to the skin est or to bronchial testing. In one of them a pul-nonary mycetoma was present and the other patient as an asthmatic. Conversely, no precipitins were found in 14 patients who reacted to *Aspergillus* extracts, although their sputum also contained *Aspergillus*.

At least 2 main antigens were present in *A. fumi-gatus* extracts as shown by the agar-gel diffusion tests with rabbit *A. fumigatus* antisera. It was shown also by tests with rabbit antisera that other species of *Aspergillus* had at least one antigen in common with *A. fumigatus*.

It was found that the amount of *A. fumigatus* material cultured from the sputum did not necessarily bear any relationship to the clinical manifestations for in some of the hypersensitive patients the fungus could be demonstrated in the sputum only after frequent examinations. It is suggested that, in such cases, precipitin tests should be performed as well as skin tests. Conversely, in cases where a skin test is positive, bronchial tests should be carried out to confirm it because skin test sensitivity may be present without a positive reaction to bronchial tests.

C. J. La Touche

NIÑO, F. L. A proposito del llamado micetoma maduromicosico del pulmon. [**Observations on the So-Called "Maduromycosis Mycetoma" of the Lungs**] *Mycopathologia.* The Hague. 1959, Dec. 30, v. 12, No. 1, 46–66, 18 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"The author presents the study of five observations of the so-called 'Maduromycosis-mycetoma of the lungs' in their clinical, histopathologic and mycologic aspects.

"The pathologic features in all these cases have been found situated in the upper lobe of the lung in bronchial cavities of women. A compact mycelial mass, 'grain', filled up these cavities.

"In one of the five cases a fungus was cultivated which was classified as belonging to the Genus *Aspergillus* MICHELII, with abnormal and atypical features.

"Short criticism is presented about the concept 'Maduromycosis-mycetoma of the lung', applied by authors designating this process."

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

WEST AFRICAN COUNCIL FOR MED. RES. **Tuberculosis and Leprosy in West Africa. Proceedings of a Conference held at Jos, Northern Nigeria, February 18th to 20th, 1959** [LEWTHWAITE, R., President]. *West African Med. J.* 1959, Dec., v. 8 (n.s.), No. 6, 213–303, illustrated. [Numerous refs.]

The first paper in this conference was the Presidential Address on *The Planning and Pursuit of Medical Research in Colonial Territories* by R. LEWTHWAITE (pp. 213–219), the Secretary of the Colonial Medical Research Committee in London. In assessing the promise of new research projects this

Committee considers particularly 4 main aspects—their objectives, and the deployment of men, funds and facilities. Lewthwaite concentrated mainly on the men, discussing the qualities (notably curiosity) which go to the making of good research workers, and on funds, which have been provided on a large scale since the Second World War [and not negligibly between the wars]. He did not say much about the choice of subjects for research beyond remarking that the advice of experienced workers is taken, and the reviewer would have welcomed more information on this important subject of what questions the research worker should be asked to answer.

In the second paper, *Tuberculosis in Nigerian Children* by O. A. SOBOYEJO (pp. 220–225), the author analyses the findings in 208 tuberculous children seen at the Lagos Chest Clinic in a period of 6 months; 124 had a history of contact. 75 had tuberculous glands, 33 had a primary complex, 58 had segmental lesions, and the remainder had various lesions. All were positive to the Heaf test; the typical picture in children referred from the out-patients department was of malnutrition, pyrexia, anaemia and dehydration; in contact children the predominant symptom was cough. In general, response to chemotherapy was very satisfactory.

In his paper on *Childhood Tuberculosis in a Rural Area of West Africa*, D. C. MORLEY (pp. 225–229), writing of experience in a Mission hospital of 120 beds in Southern Nigeria, reports that in 9 months 1,308 children were admitted, of whom 66 had tuberculosis (22 with kwashiorkor also, 18 with a primary lung lesion and the remainder with glands and other forms of the disease). The glandular element of the primary complex in the chest is more prominent than in Britain. Kwashiorkor is the most common single cause for admission. Tuberculin-positive children under 5 who are not ill enough to be admitted are started on a 6-months' course of isoniazid (10–20 mgm. per kgm.—presumably each day) on an out-patient basis, and this is usually effective.

In *Observations on the Chronicity of Pulmonary Tuberculosis in Africans*, J. E. HENSHAW (pp. 229–236) reports on 200 patients with pulmonary tuberculosis seen in the Eastern Region of Nigeria in 1954–56 and followed up since then; 150 were males and ages ranged from 16 to 60. Most patients had cavities (364 identified in the 200 patients) and 43 were classed as fibrocavitary, 63 as caseo-cavitary and 94 as other forms, some of which were cavitary. The disease was bilateral in two-thirds, and more than one zone was involved in 90%. The author does not agree that African tuberculosis is unlikely to show evidence of fibrosis—43 patients showed fibrotic disease, 46 others also showed some attempt at fibrosis, and 15 some evidence of previous healing; in 66 the disease was well localized. Chemotherapy was given and of the 364 cavities 128 remained open (112 with apparently negative sputum). The response to chemotherapy was dramatic but some failures occurred.

In his paper on *The Efficacy of Freeze-Dried BCG Vaccine in Laboratory Animals*, J. UNGAR of Glaxo Laboratories (pp. 238–244) explains the need for a vaccine which will remain viable for a long time, and how this is prepared and freeze-dried. At least 1,000 viable bacilli are needed to cause a visible local lesion after intradermal injection in guineapigs (which is the most satisfactory and consistent route), and there was no variation after storage of the freeze-dried vaccine at 4°C. for up to 3 years. Challenge with virulent organisms 6 weeks after vaccination showed that animals "successfully immunized" had only local and glandular lesions for 3–4 months, but eventually died of pulmonary tuberculosis; controls died much earlier of generalized tuberculosis.

P. P. BROWN, in *A Comparison of Various Methods used in the Laboratory Diagnosis and Assessment of Pulmonary Tuberculosis* (pp. 244–251), discusses in detail the results of examination of a large number of sputa by direct smear, by smear of sputum concentrated by means of sodium hydroxide or trisodium phosphate, and by culture after concentration. In untreated patients direct smear is almost as satisfactory as concentrate smear, but not in patients undergoing treatment. Concentration by sodium hydroxide is as satisfactory as by trisodium phosphate for smear examination but not for culture. Loewenstein-Jensen medium prepared locally was used with success; 2 tubes should be inoculated and incubated for 12 weeks before being pronounced negative. A single early-morning specimen is as reliable as a 24-hour specimen for culture. [It is irritating to see the spelling "Ziehl-Neilson" (p. 244) after all these years, and the remark that "CRUIKSHANK (1951), in relation to positive smears, gives the numbers necessary as 10–50,000 per ml." is unsatisfactory; it probably means 10,000–50,000.]

In his paper on *The Tuberculin Reaction* F. R. G. HEAF (pp. 255–257) comments on the fact that "there is still a great deal to be desired with regard to its specificity and accuracy." The intradermal test is the best for epidemiological work, but the Pirquet and Heaf tests are quite satisfactory for routine BCG work.

Not much information has been published on tuberculosis in Ghana, but the paper by W. J. BELL on *The Pattern of Symptomatic Pulmonary Tuberculosis in Ashanti, with Particular Reference to Management* (pp. 258–265) gives details of 590 cases of pulmonary tuberculosis observed in 1957, and there is little ground for complacency. Half the patients were urban, but almost one-third were rural, the remainder being semi-rural. Two-thirds were males and most patients were aged 16–39. 31% were acutely ill, 37% in poor condition; almost all had positive sputum and 43% had haemoptysis. Of 274 cultures made, 28% were resistant to one or other of the three drugs used, streptomycin, PAS or isoniazid. Most patients with sensitive organisms had not previously been treated with drugs whereas most of those with resistant organisms had. Cavities were present in 87%, mostly affecting more than one zone. 87% of the cases were classed as acute or subacute. Hospital treatment was not possible for about two-thirds of the patients, and the author reports that only 39% of the out-patients continued regular treatment for a year, and even in these the drugs had only rarely been taken in full dosage. Control of the disease in the individual "is qualified by limited therapeutic facilities, a gross symptomatic and pathological pattern of disease, and a scattered migratory population", and

' it is believed that the unplanned use of drugs (often taken in haphazard fashion) is wasteful and dangerous unless geared to an ultimate programme of surgical help in the type of disease presenting". [This is a serious paper which does not attempt to minimize the danger of the position or the difficulty of dealing with it; the author does not give many suggestions for a scheme of control.]

E. P. LINDLEY reports on *Bovine Tuberculosis in Nigeria* (pp. 266–271) noting that the highest infection rate in cattle is 7% (Southern Adamawa and the Cameroons); elsewhere, particularly in the North, the incidence is very low, of the order of 0·02%. He reports in detail on 383 tuberculous cattle—there are few records of tuberculous mastitis, and the risk to man is slight.

In his paper on *Health Education in Urban Tuberculosis Control* (pp. 273–277) O. ADENIYI-JONES made perhaps the most important contribution of all. In West Africa "we are only at the beginning of conscious planned tuberculosis control", and there can be little progress unless a sufficiently large proportion of the public understand the main principles involved. The main object of health education is to help people to achieve health by their own efforts, and for this they must accept the points of view involved. The author cites one African with tuberculosis who had been told by his medicine man that the disease was due to the machinations of a discarded wife. He decided to take her back, and was sure that he would therefore recover. He would be unlikely to obey any instructions to avoid contact with her while he believed that such contact would be essential to recovery. These are inevitable difficulties, but they need not be decisive. Effective chemotherapy will induce patients to accept institutional segregation. Compulsion would be unwise. The author wonders what would have happened if, together with research on conventional lines, it had been conducted into "the ways and means of persuading whole communities to change those health attitudes and habits which are conducive to the development of tuberculosis". He suggests that doctors should plan and direct health educational activities, official and voluntary.

V. W. J. HETREED, in a paper on *The Control of Tuberculosis in a large Tropical Town—Lagos* (pp. 277–279) estimates that in urban Africans aged over 12 years the incidence of active tuberculosis is 6 per 1,000, which means 10,000 tuberculous subjects in the towns of Nigeria; outside the large towns the rate is about 3 per 1,000 and the total about 70,000. A comprehensive control scheme would cost £500,000 to create and £250,000 a year to run. At present in Lagos a small staff carries out treatment, X-ray examination and BCG vaccination. The author expects improvements in educational and economic standards during the next few years.

In *Towards a Tuberculosis Service in Western Nigeria*, N. M. O'BEIRN (pp. 280–282) mentions that WHO teams in 1955–56 and in 1957 estimated the incidence of infective pulmonary tuberculosis at 2·6 per 1,000 for Nigeria as a whole, and 6·2 for town dwellers. There is a special clinic at Ibadan and smaller clinics at smaller hospitals. Control for tuberculin negative persons suggests BCG, for tuberculin positive but otherwise healthy persons, a heroic scheme of "prophylactic" isoniazid might be envisaged, but otherwise treatment might be given to those with small lesions revealed by mass radiography. In the discussion G. T. DUNGER of an oil company in Lagos emphasized his view that commercial establishments should ensure good wages and living conditions for their employees, and insist on periodical miniature radiography.

J. R. LAUCKNER, in *Out-Patient Chemotherapy Trials in Ibadan* (pp. 285–288) is not over-optimistic. A combination of streptomycin, isoniazid and PAS was found to give satisfactory results in 71% of 51 ambulatory patients whereas isoniazid alone and isoniazid with PAS was satisfactory in only about half that proportion or less. Many patients did not complete the full courses, for various reasons, and the author therefore advocates admission to hospital for very sick persons, or treatment at home, provision of treatment centres within the easy reach of the patients, and adequate education of the patients regarding the need for prolonged treatment. As a compromise he gives streptomycin 3 times each week for 3 months, together with isoniazid and PAS daily for a much longer period.

A. W. WILLIAMS and J. PEPYS (pp. 289–291) give an account of *East African/British Medical Research Council Tuberculosis Investigations* which were undertaken within the last few years and which showed that DDS was not sufficiently effective, when given with isoniazid, in converting positive to negative sputum. The combined use of PAS and isoniazid was better, and the authors now report (p. 291) that this treatment (10 gm. PAS and isoniazid 200 mgm. daily) is better than isoniazid alone or with pyridoxine.

J. H. MEISTER (pp. 292–295) in *Surgical Treatment of Pulmonary Tuberculosis with Limited Facilities*, writes from the Basel Mission, Agogo, Ghana, and is concerned to show that surgical procedures—thoracoplasty and plombage—can be used successfully in Africans. He records 48 thoracoplasties and 9 plombages, and the results are encouraging.

In the final paper A. B. P. W. KOCH of the Ministry of Health, Ghana, sums up *Modern Treatment of Tuberculosis and its Application under West African Conditions* (pp. 298–301). In Accra patients tend to continue treatment if injections are given and the practice is now to give streptomycin 3 times each week to a total of 90 gm., together with isoniazid or PAS or both for a year or more. *Charles Wilcocks*

AMERICAN REV. RESPIRATORY DIS. 1959, Oct., v. 80, No. 4, Pt. 2, pp. iii + 139. **International Symposium of the Deborah Sanatorium and Hospital. Philadelphia, Pennsylvania, November 20–22, 1958.**

This symposium was organized by the Deborah Sanatorium, New Jersey, as they said, to bring back Deborah into the field of medical education. As tuberculosis was the first medical interest of Deborah, this subject was chosen as the first topic. 6 panels of distinguished

medical workers from all over the world were organized to deal with various aspects of tuberculosis. Photographs of the members of each panel were taken, and are published with the symposium. These are interesting as they enable readers to become acquainted with the appearance of many experts who have previously been known to them only by name. If the idea is prevalent that the tuberculosis problem, even in advanced countries, has been solved, reading of this symposium will eradicate it. The number of problems raised was enormous, and the amount of disagreement on them among these experts was surprising. Very little new research was reported, only one or two new pieces of work being mentioned. The answers by the panel were unrehearsed, and this gave the discussion an air of spontaneity.

A good deal of time had to be expended on clarifying definitions before any progress could be made on the subject of the discussion. Anyone present who had not a considerable background knowledge of recent work on tuberculosis must certainly have found himself overwhelmed. To those who had the background knowledge, the various views put forward must have been both instructive and amusing. The panels discussed the following subjects: (1) The chemo-prophylaxis of tuberculosis. (2) The respective roles in tuberculosis management of the hospital and home, including the chemotherapy of tuberculosis. (3) The problem of relapse of tuberculous lesions under chemotherapy and after treatment. (4) Tuberculosis case finding. (5) Surgical aspects of the treatment of pulmonary tuberculosis. (6) The future problem of tuberculosis. Programme for its control.

The first subject, the chemo-prophylaxis of tuberculosis (pp. 1–21), was introduced by Sidney RAFFEL; he emphasized that he took the title to mean prophylaxis, prevention of tuberculosis, rather than early chemotherapy, *i.e.,* chemotherapy after the tuberculin reactivity had been established. It is not yet generally agreed whether prophylaxis as defined in this way is altogether advantageous. Points in favour are: (1) isoniazid is relatively non-toxic and has a high level of bactericidal activity *in vitro*; (2) long-continued use of isoniazid does not lead to disturbances of the normal flora; (3) for some reason unknown, this long continuous use of the drug does not result in the emergence of resistance in the tubercle bacilli. On the other side (1) it has been shown experimentally that infections with tubercle bacilli can be acquired by animals during the time when they are being covered by the drug administration, and that these organisms may remain present but latent; (2) after cessation of treatment these bacilli can set up active infection; (3) animals treated in this way do not develop the immunity which is normally received. To deal with this point he suggested that BCG should be used at the same time so that the individual received the drug and was immunized simultaneously.

Gardner MIDDLEBROOK reported on an investigation which showed that where 2 to 3 bacilli were given by the air-borne route to guineapigs and isoniazid was given prophylactically, all escaped infection, but where 58 bacilli were given only 8 out of 12 were protected. The tuberculin reaction did not become positive until some time after drug administration was stopped. P. D'ARCY HART felt that the size of tuberculin reaction made quite a difference in prognosis, and suggested that children with a strongly positive reaction should be given isoniazid for several years, especially about the age of 14.

In the second panel discussion on hospital and home in tuberculosis management (pp. 23–45), most speakers seemed to think that all patients should be treated in hospital initially, apart from those in whom the disease was minimal, and certainly all in whom a relapse had taken place. Home treatment *ab initio* was certainly not so popular in the United States as it appears to be in Great Britain at present. In the United States the dangers of PAS, and the difficulties in getting patients to take it, seemed to be emphasized and feared more than they are in Great Britain. The percentage of alcoholics with tuberculosis in the United States made the use of PAS very difficult unless it was given under nursing supervision. Some speakers advocated the use of thiourea instead of PAS, and, contrary to opinion in Great Britain, the use of isoniazid alone, especially in the latter part of treatment, was quite popular. Most speakers agreed that streptomycin given every day was superior to the regime in which it is given on alternate days, but from the practical point of view the use of alternate day streptomycin is very common in the United States. It was generally agreed that the length of time for which the antituberculous drugs should be given depended more on the response to the drugs than on the initial lesion. Where cases were resistant to the 3 standard drugs, the most popular regime was isoniazid with cycloserine.

J. D. STEELE in opening the third panel discussion about relapses (pp. 47–71), thought that the rate was tending to increase. The panel had great difficulty in defining "relapse" in the absence of a serological test which was satisfactory. A considerable discussion took place as to whether a relapse could be defined as such in the absence of a positive sputum; the panel finally decided that for the purposes of study, bacteriological confirmation must be required, but in practice most workers considered that this was not necessary, and they treated patients who had clinical and radiological deterioration as cases of relapse. No conclusion could be reached as to whether a high proportion of relapse cases had resistant or non-resistant organisms. J. M. ROBSON, of Guy's Hospital, London (pp. 56–59), gave an account of interesting experiments on the cornea of mice, in which it was shown that if after infection had been in progress the mice were treated with isoniazid for about 11 months, multiplication was completely prevented and spread into other organs did not occur; but all the organisms in the cornea were not killed, and immunity was prevented from developing. He thought that this lack of killing power of isoniazid was due to the fact that some of the organisms were in the resting stage.

In panel V on surgical aspects of treatment (pp. 95–115) the results from a number of surgeons in different countries indicated that thoracoplasty was on the downgrade, and recently up to 90% of the major operations were by resection. F. R. EDWARDS said that in the 50 to 60 year age-group resection was less well

tolerated, and although he still felt that it was better to perform resection he often took what he felt to be the easiest line and performed thoracoplasty. Professor SEMB said that one of the advantages of thoracoplasty was that nodular infiltrations, not only in the infected lobes but also in other lobes, tended to heal better with a thoracoplasty than by resection. The panel seemed to think that although 6 months' chemotherapy was a usual standard time before resection, quite often it was safe to proceed very much earlier. N. J. WILSON said that the earlier he did his surgery the less tuberculosis morbidity resulted. He felt that the decrease in psychological morbidity produced by early operation was of very great moment. The surprising aspect of the whole discussion was that although the length of time for which drugs should be used before operation was considered very thoroughly, the length of time for their use after an operation was not touched on by any speaker.

Panels IV (pp. 73–93) and VI (pp. 117–137) dealt with public health problems, tuberculosis case finding and control, and although interesting did not reveal any outstanding points. The great difficulty mentioned by everybody seemed to be that although what should be done was known, the human factor usually prevented it from being done, at any rate in the more advanced countries.

This type of symposium achieved its avowed result very successfully but it is unlikely that it can be repeated profitably on a future occasion.

F. H. Young

BERNARD, E., LOTTE, A. & PRETET, S. Mesure du péril tuberculeux. [**Tuberculosis Morbidity in France**] *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 21, 22 & 23, 462–71, 6 figs.

Although the death rate from tuberculosis in France has fallen from 215/100,000 in 1910 to 24 in 1958 France still has the third highest rate of 12 European countries.

The reduction has been most marked in young persons up to the age of 25 years and least marked in those aged 65–69 years. The rates are comparable in males and females up to the age of 30 but after that age females fare better than males so that at 50–60 years the rate in men is 5–6 times higher than in women.

Information about morbidity is very incomplete. In 1957, 44,000 new cases of tuberculosis of all kinds were reported by the tuberculosis dispensaries (100/100,000). Patients with primary disease showing pathological manifestations numbered 14,200. The total number of new cases is only about 60% of the number of persons who received insurance benefits for tuberculosis. It is clear that the decline in morbidity is much slower than in mortality.

Tuberculin surveys made in Paris schools in 1953–54 showed that the reactor rate was 12% at 7 years, 22% at 10 and 38% at 14. The risk of tuberculous infection is 6 times greater for a child in Paris than for a child in Copenhagen.

H. G. Calwell

KARPINOS, B. D. **Prevalence of Tuberculosis among Selective Service Registrants currently processed for Military Service.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 795–805, 1 fig. [19 refs.]

This paper deals with the prevalence of tuberculosis among selective service registrants currently processed for military service in the U.S. forces. It deals with 177,000 men within the age range of 18 to 26; the mean age was 21·5 years. The prevalence rate of disqualifying tuberculosis among these was: respiratory tuberculosis: Total (white and Negro)—18·0; white—16·2; Negro—27·9, per 10,000. Tuberculosis, all forms: Total (white and Negro) 20·3. When the number previously screened out were added 28·7 for respiratory or 32·7 for tuberculosis of all forms per 10,000 white and Negro registrants was recorded. A certain number of cases of tuberculosis are missed at the medical examinations, consequently a special review was undertaken to determine the number of registrants hospitalized for respiratory tuberculosis after induction.

It was found that 4 of 10,000 recruits can be expected to be hospitalized during their 2-year tour of military duty for respiratory tuberculosis not diagnosed as existing before service; these presumably represent cases of respiratory tuberculosis missed at the time of the registrants examination for military service. When adjusted for these latter cases the overall prevalence rates become 32·0 for respiratory tuberculosis, or 36·2 for tuberculosis of all forms per 100,000 registrants currently examined for military service. Further study indicated that the present prevalence of respiratory tuberculosis among selective service registrants is somewhat less than one-third of what it was in World War II within a comparable age range.

F. H. Young

GORDON, W. L. **Results of Tuberculin Testing and Radiography of 13-Year-Old Birmingham School Children from 1954 to 1958.** *Tubercle.* 1959, Dec., v. 40, No. 6, 466–7.

When BCG vaccination of the 13-year-old schoolchildren was started in Birmingham in 1954, 18·3% were found to give a reaction of 5 mm. or more induration to 10 TU of PPD intradermally. This has declined to only 11·9% in 1958. Children who had a particularly strong Mantoux positive reaction were given a chest X-ray without delay. Of the 1,597 patients who had a positive tuberculin reaction 727 had a strongly positive reaction and were given immediate chest X-ray. 12 cases of tuberculosis requiring close clinic supervision or immediate treatment were discovered giving a rate 16·5 per 1,000. Of the 3,360 cases remaining—tuberculin positives, and those not participating in the vaccination scheme—no cases were found to require close clinic supervision or immediate treatment.

F. H. Young

CONNECTICUT HEALTH BULL. 1959, Dec., v. 73, No. 12, 369–77, 3 figs. **Mass Tuberculin Testing Programs—Advantages and Disadvantages.**

The State Department of Health in Connecticut conducted pilot tuberculin surveys in order to explore their educational, testing, follow-up and case-finding aspects.

The first survey was made in 1956 in a rural community (population 5,000) when about 85% of the total school population of 771 students were tested. 1st and 2nd strength PPD was used by intracutaneous injection. 1·8% reacted to the 1st test and 8·6% to the 2nd. All reactors and school personnel were X-rayed. No evidence of tuberculosis was found.

The homes of reactors were visited and 150 contacts invited to attend for examination but only 67 (44·6%) did so. One of these was found to have active minimal pulmonary tuberculosis.

The next survey was made in a city of 187,000 persons in 1958. 2,288 students (87% of the total invited) were tested of whom 35 (1·5%) reacted to 5 TU of PPD. All reactors were X-rayed but no case of active pulmonary tuberculosis was found.

245 household contacts of the reactors were invited to attend for examination of whom 211 (86%) were eventually examined. 197 were tuberculin tested of whom 30% reacted, and 196 were X-rayed. No case of active pulmonary tuberculosis was discovered.

In spite of the above disappointing results the author believes that tuberculin surveys have a place in tuberculosis control programmes but not at the expense of other valuable and tested methods of ascertainment.

H. G. Calwell

WIER, J. A. & SCHLESS, J. M. **The Tuberculin Reactions of 530 Patients admitted to the Tuberculosis Service, Fitzsimons Army Hospital.** *Amer. Rev. Respiratory Dis.* 1959, Oct., v. 80, No. 4, Pt. 1, 569–74.

530 patients with tuberculosis or possible tuberculosis admitted to a military hospital in the United States of America were Mantoux tested with PPD.

Patients who did not react to the first strength (0·00002 mgm.) were immediately tested with intermediate strength (0·0001 mgm.) and if they did not react were retested with second strength (0·005 mgm.). All were tested simultaneously with histoplasmin and coccidioidin. Tests were read at 48 and 72 hours and the results recorded in mm. of erythema and induration.

The reactions were definitely positive (over 5 mm. induration) in 498 patients; 27 remained negative and were regarded as free from tuberculosis; in 5 no final classification could be made.

If all reactions to the second strength with less than 10 mm. induration are excluded as doubtful, it can be concluded that the intermediate dose should detect nearly 95% of reactors, but a negative reaction to the intermediate dose does not exclude tuberculosis, since of 32 patients negative to the intermediate dose, 23 were finally diagnosed as having active tuberculosis.

Readings at 48 hours were slightly more reliable than those taken at 72 hours.

No patient in the series with an unequivocally negative reaction to PPD was shown subsequently to have clinical tuberculosis. Several patients who reacted with erythema and indefinite induration were found to have active tuberculosis; they reacted to OT. Dubious reactions to PPD should therefore be checked by repeat testing with OT and dubious reactions to OT should be checked with PPD. For all practical purposes a negative Mantoux reaction is reliable for excluding tuberculosis. The case of infection with non-specific (chromogenic) mycobacteria is an exception.

H. G. Calwell

WIJSMULLER, G. **Naturally Acquired Tuberculin Sensitivity in Netherlands New Guinea.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 641–65, 9 figs. [19 refs.]

These studies in tuberculin sensitivity were made in Netherlands New Guinea in connexion with the WHO/UNICEF BCG vaccination programme introduced there in 1956.

The Mantoux Test was used with 5 and 100 TU of human and avian tuberculin (Danish PPD).

In a group of men from a district where clinical tuberculosis was unknown and from the population of an area where tuberculosis was rare, the reactions to 5 and 100 TU were of medium size (mode 12–14 mm.), but in a group of tuberculous patients and in the population of an area where tuberculosis was frequent, large reactions (18 mm. +) to 5 TU were common.

In children vaccinated with BCG and tested with 5 TU of human and avian tuberculin, the reactions to human tuberculin tended to be smaller than the reactions to avian tuberculin, but in tuberculous patients the reverse was the case. With larger doses (100 TU) the difference between the two tuberculins was less marked.

When the volume of fluid (and dose) injected was reduced the size of the reactions decreased, and *vice versa*; when the volume of fluid (but not the dose of tuberculin) was increased the size of the larger reactions was increased, and *vice versa*.

There are therefore several differences between strong and weak reactors, and the author suggests that the strong reactors have in general become allergic through infection with tubercle bacilli, but the medium reactors through infection with some other organism.

H. G. Calwell

BECK, F. **Pulmonary Disease due to Atypical Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 738–43. [11 refs.]

The author gives brief histories of 9 patients from whom these bacilli were grown; 1 of the patients was aged 33 years, another was aged 45 years and the remainder were aged 55 or more years. 3 of the patients had proved tuberculosis but only 1 was excreting tubercle bacilli at the time that the atypical bacillus was grown. 5 of the strains were photochromogens and of the 6 strains tested for virulence in guineapigs, none produced progressive disease. All the strains were resistant to PAS; 2 of the strains were sensitive, 3 partially resistant and 4 were fully resistant to isoniazid; 1 strain was sensitive, 4 were partially resistant and 4 were fully resistant to streptomycin.

The author stresses that the disease is indistinguishable from tuberculosis and that the diagnosis is dependent upon the bacteriologist. There was no evidence that these bacilli represent an end result of

chemotherapy for some of the patients had not been treated with antituberculous drugs nor had they been in contact with persons who had been treated with these drugs. There is no evidence that the disease is contagious, and the fact that the patients were in the older age-groups suggests that the infection arises in lungs damaged by non-tuberculous lesions, *e.g.* emphysema or silicosis. *S. R. M. Bushby*

EDWARDS, Lydia B. & PALMER, C. E. **Isolation of "Atypical" Mycobacteria from Healthy Persons.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 747–9.

This investigation was carried out on 122 persons on plantations in Georgia. Previous tuberculosis studies made on this area had shown that there was little evidence of tuberculosis but that there was a high prevalence of non-specific tuberculin sensitivity. For example in 1956 reactions of 10 mm. or more to PPD-S were found in only 2·6% of persons less than 20 years of age and in each of these persons the reaction to samples of PPD from an atypical acid-fast bacillus and avian tubercle bacilli were larger. In the adult population, 30% had a reaction of 10 mm. or more to the PPD-S but the reactions were larger to the other antigens in one-third of them.

Each of the 122 persons supplied a sample of sputum, many of which were only saliva, and from these specimens 14 strains of Actinomycetaceae, 3 strains of *Mycobacterium fortuitum*, and 13 strains of "atypical" acid-fast bacilli were isolated. These "atypical" acid-fast bacilli were identified as 3 scotochromogens (Runyon's Group II), 7 non-photochromogens of the Battey type (Runyon's Group III) 5 (including the 3 *Myco. fortuitum*) were rapid growers (Runyon's Group IV) and 1 was a mixture of Groups II and III. No tubercle bacilli were isolated.

The specimens were obtained as frequently from young persons as from older ones, and from saliva as from sputum. The positive cultures were obtained more frequently from workers of 2 farms than from those of the other farms, but no explanation for this difference was found. None of the persons with positive culture had radiological evidence of pulmonary disease.

Although this study is only small the authors maintain that the results are sufficiently suggestive that the sensitivity to the non-tuberculous PPD is due to a benign asymptomatic infection with atypical acid-fast bacilli to warrant a larger investigation.

S. R. M. Bushby

WILKENS, G. L. & TASMAN, A. **On the Immunological Reactivity of Tuberculous Patients. Preliminary Report.** *Brit. Med. J.* 1959. Dec. 12, 1305–7.

The amounts of antitoxin in the sera of 11 healthy men and women and of 16 tuberculous patients were measured at weekly intervals after the second of 2 intramuscular injections each of 5 Lf of tetanus toxoid given at from 3 to 5 weeks apart. Of the 16 patients 11 suffered from chronic tuberculosis and 5 had recently developed the disease.

The tuberculous patients produced much less antitoxin than the controls. 1 week after the second dose of toxoid 2 of 16 patients and 6 of 11 controls had more than 0·01 unit per ml. 5 weeks later 5 tuberculous patients had failed to produce detectable antitoxin. The others formed antitoxin more slowly than the controls and in most cases in smaller amounts.

These results are similar to those found by GREENWOOD *et al.* (*Brit. med. J.*, 1958, v. 1, 1388) with sarcoid patients. *I. B. R. Duncan*

JENTGENS, H. Schwangerschaft bei "inaktiver" Tuberkulose. [**Pregnancy in the Case of "Inactive" Tuberculosis**] *Deut. med. Woch.* 1960, Jan. 1, v. 85, No. 1, 24–31, 52, 5 figs. (4 on 3 pls.) [17 refs.]

Advances in the treatment of tuberculosis have brought a solution of the problem of tuberculosis and pregnancy. If the disease is active there is no doubt that specific treatment should be given without terminating the pregnancy but there is less certainty when the state of the tuberculous lesion is inactive or doubtfully active.

Illustrative examples are given of cases where in spite of a history of pulmonary tuberculosis insufficient care was taken to ensure that the disease was in fact inactive throughout the period of gestation. A single examination at the start of pregnancy may be insufficient and lead to disaster both for the mother and the infant.

The risk of reactivation of the disease in pregnant women has been estimated at 10%. In the author's series of 974 patients relapse occurred in 62 (6·3%). All women known to have had pulmonary tuberculosis should be supervised carefully during pregnancy, and if there is any doubt about the activity of the disease specific treatment should be given.

Treatment is indicated especially of those with round foci, which are notoriously unstable. An example is given. 35 pregnant women with round foci in the lungs are quoted, of whom 17 deteriorated during pregnancy and 10 of these underwent resection.

Another condition which points to the need for specific treatment is pleural effusion. In a series of 108 women with a history of pleural effusion 20 showed evidence of destructive tuberculosis during the course of pregnancy and required treatment. The same holds for those with a history of pulmonary resection within the previous 2 or 3 years.

There is great difficulty in deciding what is best to be done when there is a history of extra-pulmonary tuberculosis. X-ray examination of the lower spine or pelvis cannot be done because of the radiation risk. In cases of doubt specific treatment should be given. Urogenital tuberculosis carries a special risk for the child because of the possibility of trans-placental infection. The mother should therefore be treated.

H. G. Calwell

See also p. 344, FERRARIS & PAOLI, [**The Bronchographic Picture in Silico-Tuberculosis.**]

CITRON, K. M. & KUPER, S. W. A. **Para-Aminosalicylic-Acid (PAS) Concentrations in the Serum during Treatment with various PAS Preparations.** *Tubercle.* 1959, Dec., v. 40, No. 6, 443–52, 3 figs. [20 refs.]

The well known tendency of PAS to cause digestive upset has led to the introduction of many preparations which it is claimed cause less digestive symptoms, but it has not been determined beyond argument that all of these give satisfactory PAS serum levels. This paper compares the serum concentration of PAS during treatment with various PAS preparations, including sodium PAS, in solution, in cachets, granules, enteric coated tablets, effervescent tablets, calcium PAS, calcium benzoyl PAS and phenyl PAS. The serum PAS concentrations were estimated by the method of NEWHOUSE and KLYNE (*Biochem J.*, 1949, v. 44, vii). This method does not measure the acetyl PAS—a biologically inert substance; it does include glycine PAS, which is also probably biologically inactive, but it only amounts to 5 to 10% of the total PAS after oral sodium or calcium PAS. Preliminary studies showed that peak levels are obtained in 2 hours, so specimens of serum were taken at this time. The concentration of PAS in the serum required for the best therapeutic result is unknown, but the minimal inhibitory concentration of PAS *in vitro* is about 2 mgm.%, so that at least 2 mgm.% biologically active PAS in the serum is probably necessary. There is considerable evidence to show that 5 mgm.% in the serum is probably a safer level.

Sodium PAS cachets 5 mgm. almost always produced serum levels above 5 mgm.%, and up to 2 mgm.% persisted for 6 hours. Sodium PAS solution (1 gm. in 3·5 ml.) 5 gm. gave an average concentration of 7·5 mgm.%. No lack of efficiency was produced by keeping the solution at room temperature for up to 12 days. Sodium PAS granules 5 gm. gave an average level of 7·1 mgm.%. Enteric coated sodium PAS tablets 5·25 gm. gave an average level of 5·7 mgm, in comparison with an average level of 8·8 mgm.% in the same patients after taking 5 gm. sodium PAS cachets. Some levels were very low; maximum concentration, however, of the serum levels was later than with the other sodium PAS preparations. Effervescent sodium PAS tablets (2 tablets represent 5 gm. sodium PAS) showed an average level of 9·5 mgm.% in comparison with 6·6 mgm.% in these patients after taking 5 gm. sodium PAS in cachets. After taking 6 gm. of calcium PAS the average of 8 estimations in 4 patients was 13 mgm.%. 3·5 gm. of calcium benzoyl PAS gave a concentration of less than 0·5 mgm.%, except in 1 patient where a level of 2·3 mgm.% was found. 7 gm. were given twice daily to 6 patients, and blood taken 2 hours after the morning dose in the first, 4th, 8th, 11th day of treatment. The average of 27 estimations was only 2·1 mgm.%. The average level on the 4th day was higher than on the first; but no further increase occurred up to the 15th day.

4 patients were given a single dose of 4 gm. phenyl PAS. Average serum level 2 hours afterwards was 3·5 mgm.%, rising to 3·6 after 4 hours.

The authors conclude that serum PAS concentrations with sodium PAS in solution and cachets are equivalent to other preparations of PAS in the form of granules and effervescent tablets, and also calcium cachets. The enteric coated tablet of PAS gave low levels. Phenyl PAS gave low but steady levels. Calcium benzoyl PAS gave very low levels. In view of the dispute about the efficiency of this drug the authors have reviewed the literature and found it very conflicting [this *Bulletin*, 1955, v. 30, 673; 1959, v. 34, 120], but conclude that at present it cannot be recommended as an alternative to a conventional PAS preparation. They discuss the advantages and disadvantages of the various PAS preparations. [This is a very valuable and interesting paper.] *F. H. Young*

SEINFELD, E. & STARR, P., with the technical assistance of Margaret SIMPSON. **Studies of Thyroid Function in Patients treated with Para-Aminosalicylic Acid and Isoniazid.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 845–8.

"Prolonged ingestion of PAS and isoniazid for six months or more may indirectly stimulate the expansion of the thyroid iodide trapping mechanism, thereby increasing I^{131} uptake above average normal concentrations. The PAS is presumably wholly or predominantly responsible for the effect. The administration of isoniazid-PAS also inhibits iodine trapping by the thyroid gland, as manifested by the marked increase in thyroidal iodine uptake three days after PAS was discontinued. Prolonged administration of isoniazid and PAS may depress thyroxine production with no overt signs of goiter or hypothyroidism. All tuberculous patients on prolonged treatment with isoniazid-PAS should be observed for possible subclinical hypothyroidism."

See also p. 344, VIGLIANI & SASSI, [**Treatment of Active Tuberculosis in Silicotic Subjects.**]

SIMPSON, J. McD. **Drug Resistance in Out-Patients treated with Sodium PAS and Isoniazid Cachets.** *Tubercle.* 1959, Dec., v. 40, No. 6, 453–6. [11 refs.]

Over the last year or two it has become apparent that failure by out-patients to take PAS is very common [this *Bulletin*, 1958, v. 33, 112, 942], and as a result isoniazid is taken alone, and resistance to it occurs. An effort was made to obviate the danger by dispensing the correct proportion of both drugs in the same powder or cachet. The author reports on 12 cases (who were collected from about 2,500 out-patients) who developed isoniazid resistance when treated by this method. In 9 there was undoubtedly failure to take the combined cachet. In 2 there is some doubt, and in 1 no evidence of irregular consumption of chemotherapeutic drugs could be found. In only 1 patient was biological relapse with emergence of isoniazid resistant bacilli not accompanied by radiographic deterioration. Of the 12 patients, 9 certainly had organisms sensitive both to PAS and isoniazid at the start of the treatment. In the remaining 3 the first positive cultures were obtained after chemotherapy had been

prescribed for periods of 8 and 12 months. These showed that isoniazid resistance had been present already, sensitivity to PAS being retained. 4 of the 12 patients finally developed resistance to PAS in addition to isoniazid. The author admits that it cannot be claimed that the factors responsible for the development of isoniazid resistance in this series of 12 cases had been established with complete certainty, though the probability is very high. Apparently if a patient fails to take his full number of cachets even though the dose of isoniazid is reduced in proportion to that of PAS the amount of the latter drug may, in certain cases, prove insufficient to prevent the emergence of isoniazid resistance.

The value of this paper is that the author has shown that the use of combined PAS and isoniazid capsules is not a complete safeguard against the development of isoniazid or PAS resistance if the cachets are taken irregularly. *F. H. Young*

PHILLIPS, S. **VII. Comparison of Isoniazid alone with Isoniazid-PAS in the Original Chemotherapy of Noncavitary Pulmonary Tuberculosis. Results from the Veterans Administration-Armed Forces Co-operative Study on the Chemotherapy of Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 641–7, 5 figs.

Whether it is advantageous to add PAS to isoniazid in the treatment of pulmonary tuberculosis is the subject of considerable controversy. This paper reports a trial by the Veterans Administration-Armed Forces Co-operative Administration to determine the facts in this controversy. It is stated to be the first large-scale trial so far reported. 282 patients were available for analysis; 189 of whom had received treatment for 5–8 months.

The group chosen comprised either minimal cases or moderately advanced cases without cavitation. All cavitated cases were excluded. The groups appear to have been very fairly comparable. 7% of the patients who received isoniazid alone, and 8% of the patients who received isoniazid and PAS had resections performed. X-ray improvement seems to have been about the same in both groups. Sputum conversion defined as sputum cultures for tubercle bacilli negative for at least 3 months was about equal in both cases.

65% of the cases of minimal disease lost their infectiousness between 0 and 4 months. Between 5 and 8 months, however, there was a somewhat higher conversion rate on the isoniazid/PAS (95% as against 77%). On the other hand in patients with moderately advanced disease the conversion rate was similar at the end of 4 months, but was higher in the isoniazid alone group between 5 and 8 months (91% as against 81%) than for those treated with isoniazid/PAS. 94 of the 282 patients still had tubercle bacilli in the sputum at the 0–4 months observation point. Only 3 of these 94 patients were discharging any organisms which were resistant to isoniazid; 2 of these 3 were from the group which has received isoniazid/PAS. Details are given of these cases. At the end of 5–8 months only 28 of the 189 patients had not achieved sputum conversion; only 3 of the 28 had isoniazid resistant organisms; 2 of the 3 from the group which received isoniazid alone. Thus isoniazid resistance was only found in 6 patients; 3 on each of the regimes. 5 of them had moderately advanced disease, and in 1, in the isoniazid/PAS group, there was an unidentified cavity found at operation.

At 0–4 months, 17 patients (11%) of those on isoniazid/PAS regime developed PAS toxicity, but of these 3 were thought to have developed toxic symptoms due to isoniazid. No patient in the isoniazid alone group developed toxicity sufficiently severely to necessitate change of treatment whereas in the isoniazid/PAS group toxicity was sufficiently severe to force change of therapy in 10%. The irregular discharge rate was 11% on the combined therapy, and also on the isoniazid alone; at 5–8 months it was lower on the isoniazid alone (5%) than it was on the combination (11%).

This appears to have been a very well conducted trial and the results may be taken as authoritative. It must be emphasized, however, that cavitated cases were excluded from the trial. In the one case in which a cavity was found subsequently isoniazid resistance developed. *F. H. Young*

DAVID, J. D. P. & LEAHY, D. J. **Safe High Dosage Isoniazid Therapy.** *Brit. J. Dis. Chest.* 1959, Oct., v. 53, No. 4, 390–99. [50 refs.]

This article commences by listing the main effects of isoniazid toxicity. A table is given of the neurological symptoms of isoniazid therapy as described by various authors, and a second table detailing the neurological signs. Mention is made of the psychotic phenomena which have been reported and it is noted that schizoid personality seems particularly vulnerable. The results of 90 patients treated in hospital with higher doses of isoniazid are given. The doses given varied from 8 to 16 mgm. per kgm. body weight per day. Vitamin B complex tablets 4–6 daily were given as a safeguard in the form of Becosym (Roche); and in those patients who were given very high doses or who suffered from malnutrition, long standing tuberculosis or diabetes, a dose of 50–200 mgm. pyridoxine was given daily, depending on the severity of the case. Duration of the high dosage isoniazid treatment extended from 3 to 9 months. Elderly patients seemed to tolerate the higher dosage well. 3 patients showed toxic effects from isoniazid. The first, a female aged 31 years, developed hesitancy of micturition followed 3 days later by dryness of the mouth, constipation and twitching of the muscles of the left thigh. No neurological abnormalities were found. The isoniazid was reduced to 300 mgm. daily and pyridoxine 50 mgm. daily was given. The symptoms disappeared after 3 days treatment and 43 days later the isoniazid was increased to 600 mgm. daily, with pyridoxine 50 mgm. daily without further complications over a period of 4 months. The second patient, aged 43, developed symptoms in spite of having received 50 mgm. of pyridoxine daily. Hyperaesthesia developed but disappeared when the pyridoxine was increased to 300 mgm. daily; 2 months later it recurred,

but when the isoniazid was reduced to 300 mgm. daily the symptoms disappeared. The third, aged 63, developed twitchings of the muscles round the right ankle, and hyperaesthesia over the dorsum of both feet. This progressed in spite of the use of pyridoxine 50 mgm. daily. Reduction of the isoniazid to 300 mgm. daily led to the disappearance of the neurological signs and symptoms, but she refused further anti-tuberculous treatment.

In a discussion it is suggested that a number of patients, possibly 30%, are rapid inactivators of isoniazid [this *Bulletin*, 1957, v. 32, 1041; 1958, v. 33, 218] and it is in these cases where the high dosage system is valuable. Unfortunately, there is no very satisfactory routine test possible for the ordinary laboratory to detect these rapid inactivators and on the strength of this it is suggested that routine use of the high dosage system is advisable.

The authors discuss the type of cases in which the high dosage system is particularly indicated. These are patients with large cavities in whom it is possible that the isoniazid does not easily penetrate, and those in which tubercle bacilli are partially resistant to isoniazid. If the high dosage system is used for elderly patients it is necessary to give vitamin B complex, particularly pyridoxine before, during and after the period of high dosage isoniazid treatment. Alcoholic patients and tuberculous diabetic patients are more liable to develop peripheral neuritis, and high dosage of pyridoxine is essential especially before starting isoniazid therapy.

The authors conclude that is reasonably safe to give isoniazid in higher doses than usual in Britain provided it is covered by vitamin B complex or pyridoxine. [This is a useful paper; apart from the investigation the effects of the high dosage system, it gives a review of the literature which it is not easy to collect from elsewhere.] *F. H. Young*

JENNE, J. W. **Studies of Human Patterns of Isoniazid Metabolism using an Intravenous Fall-Off Technique with a Chemical Method.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 1–8, 3 figs. [13 refs.]

UNITED STATES PUB. HEALTH SERVICE. **Controlled Clinical Trial of Streptovaricin-Isoniazid. Tuberculosis Therapy Trials.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 757–9, 3 figs.

This note reports a pilot trial of the therapeutic efficacy of streptovaricin [this *Bulletin*, 1957, v. 32, 802, *ter*] in combination with isoniazid with isoniazid-PAS as a controlled regime. When the study was closed 79 patients who had received isoniazid-streptovaricin, and 251 patients who had been given isoniazid-PAS were available for analysis. Nearly 31% of the patients on each regime did not finish 32 weeks' treatment of assigned therapy for reasons unrelated to their disease or chemotherapy. 16 patients receiving isoniazid-PAS developed toxic reactions severe enough to require a change in the assigned regime. 2 patients (0·8%) could not tolerate isoniazid, 13 (5·2%) were intolerant to PAS, and 1 was apparently unable to take either drug. No toxic reactions were reported in the streptovaricin-isoniazid group except from those receiving 1 batch of the drug which was shown to contain impurities. 5 patients (6·3%) who received isoniazid-streptovaricin, and 2 patients (0·8%) receiving isoniazid-PAS became critically worse during treatment, and a change of regime was necessitated.

The analysis for the X-ray change was based on 158 patients who received isoniazid-PAS, and 49 patients who received isoniazid-streptovaricin. At the end of 20 weeks there was little difference in the percentage of patients who showed substantial X-ray improvement on either regime. The patients who received PAS continued to improve, while patients on streptovaricin made no further progress. At the end of 32 weeks 70·5% of the patients on the streptovaricin regime showed substantial X-ray improvement as compared with 80% of the patients on the PAS regime. Sputum conversion was slower in the patients on the streptovaricin regime and after the 16th week, no further change was observed among patients receiving isoniazid-streptovaricin. At the end of 32 weeks 33% of the patients who were receiving streptovaricin were still excreting tubercle bacilli in contrast with 7% of patients on PAS. After 28 weeks of treatment 21·6% of the patients on the streptovaricin regime had organisms resistant to at least 0·2 μgm. of isoniazid compared with only 2·8% of the patients receiving isoniazid-PAS. There was no evidence of irregular consumption.

F. H. Young

RAVAZZONI, C., SADOWSKI, L. F. & SCARPONI, F. Contributo alla conoscenza dell'attività clinica antitubercolare della sulfoniazide. [**A Contribution to the Knowledge of the Clinical Action of Sulphoniazide in Tuberculosis**] *Lotta c. la Tubercolosi.* 1959, July–Aug., v. 29, Nos. 7/8, 943–54, 8 figs. [13 refs.]

From the Chest Division of the Genoa Hospital Service, the authors relate their experience of treating with sulphoniazide [a combination of isoniazid and a sulphone] 32 patients suffering from pulmonary tuberculosis in variously advanced stages. These patients had become resistant to, and had ceased to derive any clinical or bacteriological benefit from the 3 chemotherapeutic agents in more general use, namely, streptomycin, PAS and isoniazid.

3 of the patients had diffuse, progressive, nodular lesions and the other 29 had stationary, or only slowly progressive, ulcero-fibrotic or ulcero-caseous, sometimes diffuse, often bilateral, lesions. The changes in most patients had progressed beyond much hope of reversal. The lesions were 6 to 14 months old in the 3 patients with nodular tuberculosis; the disease in the other patients had lasted from 1 to 31 years. All were men, aged 35 to 64 years.

To 14 patients all the sulphoniazide—3gm. (12 tablets) per day—was given by mouth. The other 18 patients were given only 2gm. (8 tablets) by mouth and this was supplemented by 2 phials of 0·8gm. each injected intravenously—making a daily dose of 3·6gm. altogether.

The average duration of treatment was 125 days; most patients received the drug for 5 months.

Blood examinations, including measurement of sedimentation rates, were carried out fortnightly, there were other routine laboratory and X-ray investigations monthly and the infective organism was sought in sputum and stomach content, both directly and after culture, at regular intervals. 3 patients were bacteriologically negative after 1 month of treatment, and 9 of 27 patients (33·3%) were negative after 3 months. X-rays showed impressive improvement and the drug was well tolerated. *J. Cauchi*

MAZZINI, C. & PISANU, A. Sugli effetti collaterali della terapia con cicloserina nel trattamento della tubercolosi polmonare. [**The Side Effects of Cycloserine Therapy in the Treatment of Pulmonary Tuberculosis**] *Lotta c. la Tubercolosi.* 1959, July–Aug., v. 29, Nos. 7/8, 961–70. [29 refs.]

The authors administered cycloserine to 41 men and 18 women, whose ages varied between 19 and 63 years and who had already been treated for pulmonary tuberculosis with the more generally used specific chemotherapeutic agents—streptomycin, PAS and isoniazid—and had developed resistance to these drugs. Each patient was given an initial dose of 250 mgm. daily and this was increased every third day up to a daily dose of 1 gm. cycloserine, but with some patients the maximum dose had to remain at 500 or 750 mgm. because there were signs of intolerance with higher doses. The drug had to be withdrawn within a few days from 5 of the patients who could not tolerate it; in the others the duration of treatment varied between 16 and 314 days.

There were side effects noted in 19 patients—pyrexia in 2, haemoptysis in 2, anxiety state in 2, somnolence in 2, tremors in 2, headache in 3, vertigo and pruritus in 1, blood in the sputum of 2 and a psychosis in 2 others. These last 2 cases are described; their psychotic attack came on after 2 months of cycloserine treatment and was serious enough to necessitate admission to a psychiatric ward. The drug had to be discontinued in one patient with pyrexia, but was only suspended and then resumed in the other. In the 2 cases of haemoptysis, the bleeding reappeared when the drug was resumed after having been withheld for a period. The states of anxiety, which appeared early in the course of cycloserine treatment, were sufficiently serious to contraindicate further use of the drug. The other patients who showed side effects were able to resume cycloserine treatment after only a temporary suspension. *J. Cauchi*

MAZZINI, C. & PIZZARELLI, R. La cicloserina nel trattamento della tubercolosi cavitaria resistente agli usuali medicamenti chemio-antibiotici. [**Cycloserine in the Treatment of Pulmonary Tuberculosis with Cavitation after the Development of Resistance to the more commonly used Chemo-Antibiotic Drugs**] *Lotta c. la Tubercolosi.* 1959, July–Aug., v. 29, Nos. 7/8, 1051–74, 10 figs. [63 refs.]

Cycloserine was given to 41 men and 18 women, whose ages varied between 19 and 63 years and who were suffering from chronic pulmonary tuberculosis. All these patients had already been given streptomycin, PAS and isoniazid over a long period and had become resistant to these drugs [see above].

The present paper briefly describes each case with details of cycloserine and previous treatment. The drug had to be discontinued for 5 patients because of intolerance.

For the 54 patients who received cycloserine over a sufficiently long period the results are summarized as follows:—

7 (13%) were "much improved"—their cavities disappeared, there was a marked regression of the infiltrative and exudative processes and the sputum became negative.

14 (26%) "improved"—cavities and infiltrative and exudative processes were all greatly reduced.

14 (26%) showed a "moderate improvement"—with some reduction of cavitation and of specific infiltration.

12 (22%) showed no change in the X-ray picture.

3 (5%) became worse.

2 (4%) died.

2 (4%) developed serious psychotic complications after having received cycloserine treatment for 54 and 64 days respectively and shown considerable improvement in their chest conditions. *J. Cauchi*

MORRISSEY, J. F. & RUBIN, Ruth C. **The Detection of Pyrazinamide-Induced Liver Damage by Serum Enzyme Determinations.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 855–65, 1 fig. [27 refs.]

"Hepatic toxicity is a frequent complication of pyrazinamide therapy. The serum glutamic oxalacetic and the serum glutamic pyruvic transaminase determinations are very sensitive tests to detect its presence. Significant enzyme elevations suggesting liver injury appeared in 19 of the 102 courses of pyrazinamide administered to 95 patients. Four of these patients were later shown to have developed a specific hypersensitivity to pyrazinamide. It is believed that the pyrazinamide-treated patient followed by determination of either the serum glutamic oxalacetic or the serum glutamic pyruvic transaminase at two-week intervals receives optimal protection from serious liver damage insofar as can be provided by presently available liver function tests. The serial use of transaminase determinations will help prevent serious and fatal instances of drug toxicity. Either the serum glutamic oxalacetic transaminase or the serum glutamic pyruvic transaminase determinations can be used. The serum transaminase has been found to be a simple, economical, reliable laboratory test which can be performed in most clinical laboratories."

SOMNER, A. R. **2-Ethylisothionicotinamide ("1314") in Pulmonary Tuberculosis: a Controlled Trial of Drug Tolerance.** *Tubercle.* 1959, Dec., v. 40, No. 6, 457–61.

Encouraging results have been reported with the use of 2-ethylisothionicotinamide ("1314") in the treatment of pulmonary tuberculosis [this *Bulletin*, 1959, v.

34, 620] but drug intolerance has been noted frequently. This paper reports a double blind trial of this substance from the point of view of drug tolerance. Little criticism can be made of the method of the trial, and the results can be accepted as authoritative as far as they go. Nausea was practically the only untoward symptom but it was fairly severe; vomiting was infrequent with "1314" in any dosage, occurring in 20 to 25% of patient-weeks (the unit of study) only. The results show that nausea was experienced in about one-quarter of the patient-weeks when the daily dose was 0·5 gm. of enteric coated tablets; in half the patient-weeks with 0·75 gm. and 1 gm. daily, and one-twelfth of the patient-weeks on controlled tablets. The author considers that the frequency with which treatment was interrupted was a reasonable indication of the degree of objection to the treatment. Interruptions occurred only twice in 59 patient-weeks studied on controlled tablets, twice in the 20 patient-weeks on 0·5 gm. of "1314", but rose to 13 of the 35 patient-weeks when 0·75 gm. or 1 gm. "1314" was given. *F. H. Young*

GUPTA, S. K., HOLLINGWORTH, A., ALAM, J., WILLIAMS, H. O., CRAIG, J. W., WINFIELD, B. J. & DAVIES, P. **Toxic Hazard from "1314".** [Correspondence.] *Brit. Med. J.* 1960, Jan. 2, 58.

This letter describes certain symptoms of toxaemia noted in 2 patients under treatment with "1314" [this *Bulletin*, 1959, v. 34, 620]. Most reports of toxic reactions from this drug have been of nausea and sometimes vomiting. In the first case, a man under treatment with "1314" (500 mgm. daily) and pyrazinamide (2·5 gm. daily) complained of increasing nausea and vomiting and some abdominal pain after 3 weeks' treatment. He had a tachycardia, and, on sitting up, fainted. The supine blood-pressure was 110/75. Withdrawal of the drugs led to disappearance of the symptoms. 2 weeks later, a test dose of 125 mgm. of "1314" was administered. 4 hours later he had a recurrence of abdominal pain and vomiting, with nausea, sweating, dryness of mouth, and pallor of skin. A few hours later he was still sweating, with a tachycardia, and the supine blood pressure was 110/70 mm. Hg. On suddenly changing to the sitting position, he fainted and his blood pressure dropped to 80/50 mm. Hg.

The second patient was treated with "1314" and cycloserine. Her blood pressure was 120/70. After 2 weeks on the combined drug therapy in the usual dose ("1314" and cycloserine 500 mgm. each) she was noted to be drowsy. Her symptoms were similar to the first case. Her supine blood pressure was 100/70 mm. Hg, and all drugs were withdrawn. A week later a test dose of about 65 mgm. of "1314" was given. The symptoms recurred, and even after 24 hours her supine blood pressure was 110/70 mm. Hg, and on her suddenly standing up it dropped to 90/60. She refused further treatment with "1314".

These 2 cases suggest to the authors a similar effect to that of the so-called ganglion-blocking agents.

F. H. Young

TSAI, S. H., COHEN, S. S. & YUE, W. Y. **Bronchographic Patterns following Resection for Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 26–42, 23 figs.

LOTFI, A. H., BEHAIRY, G. El Din & ABD-EL-AZIZ, A. **Practical Observations on B.C.G. Vaccination in Egyptian Infants (with a Report of 150 Complicated Cases).** *J. Egyptian Med. Ass.* 1959, v. 42, Nos. 4/5, 347–60, 21 figs. on 6 pls.

BCG vaccination of infants has been compulsory in Egypt since 1957. The authors have seen 150 cases of "major lymphadenitis" in vaccinated infants since that time.

Cervical glands were affected in 13 infants, axillary and cervical in 11 and axillary in 126. The mode of presentation was: soft 68; sinus 13, ulcer 10 and firm 56. In the last category 13 glands softened and were aspirated, 29 softened and ruptured and 14 resolved without suppuration.

Biopsy was done in 1 case of lymphadenitis without softening. The naked-eye appearance was of multiple discrete tubercles. Aspirated pus or caseous material was examined bacteriologically and the results in 60 cases were: no pyogenic organisms were found in any specimen, acid-fast bacilli were seen on direct examination in 6, tubercle bacilli were grown by culture in 45. Experimental animals inoculated with the pus showed no evidence of tuberculosis, which indicates that the organism was BCG.

Local chemotherapy was used for large ulcers; streptomycin was injected into abscess cavities after aspiration of the pus. Oral or parenteral chemotherapy was used when the general condition of the child was seriously affected or where there was combined cervical and axillary lymphadenitis or generalized lymphadenitis.

H. G. Calwell

NÈGRE, L., BRETEY, J. & ROY, D. Allergie à la tuberculine, infra-allergie aux corps bacillaires et résistance anti-tuberculeuse des cobayes vaccinés par la voie buccale avec de grosses doses de BCG. **[Resistance to Infection and Sensitivity to Tuberculin and the BCG Test in Guineapigs Vaccinated Orally with BCG]** *Bull. Acad. Nat. Med.* 1959, v. 143, Nos. 21, 22 & 23, 476–8.

Guineapigs were given 50 mgm. of BCG orally every day to a total of 250 mgm. 2 or 3 months later and at 5, 7 and 9 months they were Mantoux tested with 500 TU of OT, and those that did not react or had ceased to react were skin tested with killed BCG (75 mgm./cc.).

Only 5 (14%) of 35 reacted to OT and 11 of 28 non-reactors reacted to the BCG test (39%). The total reactor rate was therefore 45%. It was found that sensitivity was slow to appear and was elicited in a large proportion only by the BCG test. It was weak and tended to disappear at 7–9 months after vaccination.

The 35 vaccinated animals and 37 controls were inoculated with 0·001 mgm. of a bovine tubercle

bacillus 6–10 months after the vaccination. All were killed about 2 months after infection when the controls showed signs of generalized tuberculosis. There were no or only scanty tubercles in the spleen, liver and lungs of the vaccinated animals, and no difference in their resistance could be seen whether they were reactors to tuberculin or to BCG or were non-reactors. *H. G. Calwell*

VENEREAL DISEASES

GARSON, W. **Recent Developments in the Laboratory Diagnosis of Syphilis.** *Ann. Intern. Med.* 1959, Oct., v. 51, No. 4, 748–58, 1 fig. [26 refs.]

This article is essentially a critical evaluation of the newer *Treponema pallidum* tests for syphilis. The author first points out that though rates for syphilis in U.S.A. fell rapidly from 1947 to 1955, after that date they became steady or even rose slightly. The main problem at the present time is to find cases of latent syphilis and to distinguish these from biologically false positive reactors.

He lists 9 treponemal tests for syphilis and divides them into 3 categories—(1) those using whole body virulent treponemes, (2) those using a chemical fraction derived from these and (3) those using a chemical fraction from Reiter treponemes; these are subdivided into 11 different test procedures. Each is considered separately in some detail and its advantages and drawbacks pointed out; the cost, especially that of the various antigens, is of interest; the cost of the TPI test varies from 30 to 100 dollars, antigen for the TPCF test costs 3 dollars per dose but the RPCF test costs only 2 cents per dose. Several of these tests are not yet generally available.

It is pointed out that a good knowledge of these varied tests is essential for their interpretation. Thus the RPCF tends to become positive first followed by the TPCF, the reagin test and last of all the TPI; however the reagin test is the first to show signs of returning to negativity.

Attention is drawn to the Rapid Plasma Reagin (RPR) test; this will give a result within 10 minutes of withdrawing the blood and is slightly more sensitive than the VDRL slide test.

The tests referred to are: the treponema pallidum (TP) immobilization test, the TP agglutination test, the TP immune adherence test, the TP complement-fixation test, the TP methylene blue test, whole-body complement-fixation test, Reiter protein complement-fixation test, TP Wassermann test, fluorescent treponemal antibody test and TP cryolysis protein test.

T. E. Osmond

BOIRON, H., CASTETS, M. & PLAGNOL, H. Résultats de recherches effectuées sur la sérologie de la syphilis et la protidémie chez les Africains de Dakar. **[Results of Research in the Serology of Syphilis and Proteinaemia among Africans in Dakar]** *Bull. et Mém. École Nat. Méd. Pharm. de Dakar.* 1958, v. 6, 202–11. [43 refs.]

The problem presented here is why do these Africans give positive serum reactions for syphilis 20 times as often as white persons when both yaws and clinical syphilis are rare. [Later in this article positive serum tests are said to be 10 times more frequent in Africans than in whites.] One explanation is that serum proteins show a higher level in the former with lowering of the albumin and increase of the globulins especially the γ globulins.

These authors investigated 300 African women with their 307 infants; of the women 265 gave negative and 35 positive serum reactions (Kolmer, Kline and VDRL); of the infants 275 were negative and 32 positive at birth (cord blood); the 265 sero-negative mothers gave birth to 271 sero-negative babies. The 35 sero-positive mothers gave birth to 32 sero-positive and 3 sero-negative babies; 20 of these 32 babies became sero-negative without treatment in 4–8 months. Compared with normal African men the sero-negative mothers showed a lowering of total serum protein and of albumin with an increase of α and β globulins and a slight diminution of γ globulins; sero-negative babies showed more serum albumin than their mothers but less α, β and γ globulins (as do white babies).

19 sero-positive mothers showed a slight increase of total proteins, lowering of albumin and increase of γ globulins compared with sero-negative mothers; sero-positive babies showed lower total protein and higher globulin, and diminution of albumin and A/G ratio than sero-negative babies.

The authors are convinced that there were no false positive reactions among their serum tests and that all the babies were free from syphilis; therefore seeing that clinical syphilis is rare in Dakar the sero-positive mothers were probably suffering from latent yaws, which, though rare in Dakar, is prevalent in the hinterland; the differential diagnosis between yaws and syphilis is set out in detail and though the former is never congenital it may attack the nervous system and pathological features are almost identical; cross-immunity is almost complete. *T. E. Osmond*

LI, Hung-Chiung, MA, Hai-Teh, FAN, Lien-Chieh, LIU, Chi-Ho, WANG, Shuang-Yuan, SUN, Mu-Yung & TENG, K. **Syphilitic Juxta-Articular Nodes. Analysis of 103 Cases.** *Chinese Med. J.* Peking. 1959, Sept.–Oct., v. 79, Nos. 3/4, 348–53.

These authors investigated 103 cases of juxta-articular nodes occurring in patients in China, suffering from syphilis; the incidence varied from 5·3% to 0·35% of syphilitics according to the area of the country involved; the two sexes were almost equally affected and most cases occurred in patients over 30 years; the onset was usually late in the disease, *i.e.* after 4 years but rarely in the early stages; the duration of the lesions varied from 3 months to 43 years.

The sites of predilection were the coccygeal, elbow, ischial and sacral regions in that order and lesions were often multiple. Their chief characteristics were: near joints, subcutaneous, cartilaginous, painlessness, slow growth and lack of tendency to break down. Other signs of syphilis were usually absent but filariasis was also present in 22 and leprosy in 3.

Classical serum tests for syphilis were invariably positive and *Treponema pallidum* was found in one case. Reaction to treatment was usually satisfactory. The microscopical picture showed dense fibrosis with cellular infiltration, swelling of the vascular endothelium and perivascular round cell infiltration. There appears to be some evidence that the condition may rarely be congenital.

Differential diagnosis is from yaws, rheumatism, cysticercosis, xanthoma tuberosum, calcinosis, filariasis, leprosy, tuberculosis and aspergillosis. *T. E. Osmond*

LAMBOTTE, R. De l'utilité des cultures dans l'étude des affections à *Trichomonas vaginalis*. [**The Use of Cultures in the Study of Trichomonal Infections**] *Bruxelles Méd.* 1959, Nov. 22, v. 39, No. 47, 1501–6. [10 refs.]

Trichomonas vaginalis was found in 17·1% of all gynaecological consultations in Liège and in 35·4% of patients with leucorrhoea; of those infected 75% showed vaginitis and 25% were symptomless.

In the antenatal service *T. vaginalis* was found in 34·3% of all cases and in 48·8% of those with leucorrhoea; among those infected 72·7% showed vaginitis and 27·3% had no symptoms [? signs].

Thus the infection was twice as common in pregnant as in non-pregnant women; the increase of extracellular polysaccharides and decreased personal hygiene may explain this.

Direct examination and stained films are not adequate for a study of this parasite; this author therefore prepared a culture medium as follows: peptone broth, sugar (maltose, glucose, glycogen), extract of liver as a growth factor, a reducing agent to produce partial anaerobiasis, ascorbic acid, 10% horse serum sterilized by filtration, and penicillin and streptomycin to check bacterial growth. Cultures can be maintained for 7 days but tend to die out after 5 subcultures; however, if to 9 ml. of this medium is added 0·5 ml. of a killed culture of *Escherichia coli* in broth, subculture is possible and *T. vaginalis* change, in shape and appearance, showing vacuoles in round forms which contained granules; the addition of 1 ml. of fresh serum reactivates the parasite.

Of 202 specimens examined 87 were positive by culture and only 38 by direct examination; cultures were positive in 17 subjects from the cervix, in 40 from the anterior urethra and in 25 from Bartholin's gland when direct smears were negative. After the vaginitis had cleared up *T. vaginalis* was found in 6, 17 and 13 cases respectively showing that treatment does not prevent successful culture.

It was found that *T. vaginalis* was much more prevalent in the intermenstrual than in the menstrual cycle and that cultures in both cases were far more frequently positive than direct smears.

Iturine, an antibiotic produced by *Bacillus subtilis*, in a concentration of 125 μgm./ml. partially, and of 250 μgm./ml. completely, inhibits growth of *T. vaginalis*; aureomycin at 125 μgm./ml., oxytetracycline at 500 μgm./ml, bacitracin at 1,000 μgm./ml., actinomycin at 200 μgm./ml., and chloramphenicol at 125 μgm./ml. all inhibit growth, but oleandomycin even at 1,000 μgm./ml. has no effect. *T. E. Osmond*

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

ARCH. BELGES MÉD. SOCIALE, HYG., MÉD. DU TRAVAIL ET MÉD. LÉGALE. 1959, June, v. 17, No. 6, 397–475, 4 figs. [Numerous refs.] [**Symposium on Immunization.**] [In French.]

R. MANDE, A. HERRAULT and C. LEVY-MARCHAL. *"Booster" doses of vaccines in infancy* (pp. 397–407).

This is a general discussion of the value of late repeat doses of diphtheria, tetanus and whooping cough prophylactics and the possibility of usefully associating these with poliomyelitis vaccine. The change in the situation in respect of relative absence of naturally acquired diphtheria immunity in adult life because of the lack of repeated exposures to infection is emphasized, and the advantage of administration of tetanus anatoxin rather than antiserum to those already immunized and exposed to risk on account of dirty wounds is underlined.

The importance of rapid flooding of the system with antibody when a late injection of anatoxin or other prophylactic follows early immunization is generally accepted; but neither the percentage of individuals who react in this way nor the duration of this excitable state in the antibody generating equipment of the subject is known.

M. DJURISIC. *Influence of associated vaccines on the immunogenic effect of the BCG vaccine* (pp. 408–412).

Immunization was carried out with BCG vaccine alone and in different groups of animals (guineapigs) with mixtures of BCG and whooping cough vaccine,

diphtheria anatoxin and with vaccine of *Salm. typhi* and with a mixture of the 2 last.

All animals receiving BCG either alone or in these combinations were found to be protected from a subsequent infection of virulent tubercle bacilli whereas controls, with 1 exception, died with extensive tuberculous lesions.

Ch. Merieux. *Combination of anatoxins with anti-poliomyelitis vaccine and simplification of the programme of vaccinations* (pp. 413–418).

Evidence for a good response to a combined vaccination against tetanus and poliomyelitis is given. Among 7 volunteers, 4 reacted well to the polio injection and 4 to the tetanus.

A formidable programme of community vaccination is proposed, beginning in the prenatal stage and covering tetanus, diphtheria, poliomyelitis, enteric, tuberculosis, whooping cough and variola.

K. Rauss, L. Rethy, I. Ketyi and J. Maroczi. *Investigations of the immunizing action of tetanus and dysentery antigens when combined with repeat doses of other antigens* (pp. 419–432).

In view of the extensive practice of protective vaccination in Hungary, it seemed to the authors to be of special importance to check the finding of Barr and others [this *Bulletin*, 1953, v. 28, 484; 1955, v. 30, 826; 1956, v. 31, 993] that where a combined vaccination included antigens to which the subject had responded earlier, then the reaction to the antigens newly introduced suffered.

The observations were made mainly on groups of children inoculated with dysentery bacteria alone or with dysentery bacteria associated with diphtheria, tetanus and pertussis antigens in case of children already reactive to one or more of these. The response to the dysentery vaccine was estimated by the development of serum antibodies capable of protecting mice from intraperitoneal injections. The responses of the children given the simple dysentery vaccine were slightly better than those of the children receiving mixed vaccine but the differences did not appear to the authors to be significant.

K. Rauss, L. Rethy, I. Ketyi and I. Jco. *The part played by length of interval between first and second doses of vaccine with the use of polyvalent antidysentery and combined antidysentery typhoid tetanus vaccination* (pp. 433–446).

These observations led to the conclusion that there was a definite advantage in extending the interval between successive vaccinations from 2 to 4 or 6 weeks. This advantage was definite for antidysentery injections, definite and statistically significant for tetanus anatoxin but not tangible in the case of antityphoid response. In view of the marked primary response to a single injection of typhoid vaccine this is not very surprising.

R. Backhausz, G. Veres and I. Veto. *New method of passive haemagglutination in estimating the potency of diphtheria antitoxins and anatoxins* (pp. 447–468).

A very full description is given of methods and results in preparing human red cells with anatoxin after preliminary treatment of the cells with trypsin and papin. Such enzyme-treated erythrocytes are very readily coated with toxin or anatoxin and their agglutination can be used as an indication of the antitoxin content of sera. It is claimed that the method is preferable to the earlier one in which the erythrocytes were treated with tannin before coating with antigen.

J. W. McLeod

HOSPITAL AND OTHER CROSS INFECTIONS

Edebo, L. & Laurell, G. **Hospital Infection of the Urinary Tract with *Proteus*. A Clinical-Bacteriologic Study with special reference to Modes of Infection.** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 1, 93–105, 6 figs. [22 refs.]

During 1 year 125 cases of hospital infection of the urinary tract with *Proteus* were recorded in a hospital in Uppsala, Sweden. 161 of 194 strains were sensitive only to chloramphenicol and furadantin; the resistant strains could be subdivided into 4 "types" by use of the Dienes phenomenon (*Proc. Soc. Exper. Biol. & Med.*, 1946, v. 63, 265). *Proteus* strains of the "hospital" types were found on rectal thermometers and on the soap used for washing them, as well as on bedpans, and, on 5 occasions, on the hands of members of the staff; they were also found on a few sedimentation plates exposed under the beds of infected patients.

Proteus strains were found in the rectum of about 20% of patients examined soon after admission to the hospital (many of the positive patients had been in the hospital within the past year), but in nearly 100% of those who had been in hospital for more than 2 weeks.

There was no seasonal change in the incidence of *Proteus* urinary infection nor any great difference between medical and surgical wards. Of the 125 patients, only 10 had had no chemotherapy before the onset of the infection. 20 patients had fever over 39°C. 18% of the patients died from various causes; post-mortem examination almost always showed pathological changes in the urinary tract attributable to the infection. 1 patient died at a result of *Proteus* septicaemia and in 5 others *Proteus* infection probably contributed to death.

The authors consider that indirect infection by contact with nursing utensils was the principal mode of spread and they stress the potential importance of the rectal thermometer; in a comparable study in Britain in which self-infection was thought to be important, [Story, this *Bulletin*, 1955, v. 30, 356], rectal thermometers were not much used.

Antibiotic treatment did not seem to predispose to infection in the individuals, but has clearly operated to select the highly resistant strains characteristic of the hospital. *R. E. O. Williams*

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

COBURN, A. F. **The Hemolytic Streptococcus Concept in Rheumatic Fever. Clinical Art in Medical Science.** *Arch. Intern. Med.* 1959, Dec., v. 104, No. 6, 1021–9. [30 refs.]

LEPPER, M. H. & SPIES, H. W. **Treatment of Pneumococcic Meningitis. Results when Penicillin was used alone compared with those when Penicillin and Streptomycin were used together, with and without Hydrocortisone: Alternate Patient Studies.** *Arch. Intern. Med.* 1959, Aug., v. 104, No. 2, 253–9. [22 refs.]

68 patients of all ages, diagnosed as having pneumococcal meningitis, were treated alternately, as far as the time of diagnosis permitted, with penicillin alone given intravenously in the first 5 days, and with penicillin plus streptomycin intramuscularly; 37 were treated in the first group and 31 in the second. The dosage is described as follows:

"1. *Penicillin Group.*—Potassium penicillin G, 10,000,000 units daily as a continuous intravenous drip, was given to children under 12, and 24,000,000 units daily, to older children and adults. On the fifth day if the patient was doing well or at any later day in the patient who responded more slowly, 600,000 units of procaine penicillin in aqueous suspension was given at six-hour intervals. On the next day the latter drug was continued and the intravenous medication discontinued. The patient was treated for at least seven days after the temperature had permanently fallen below 101 F rectally.

"2. *Penicillin-Streptomycin Group.*—Penicillin, used as above, plus streptomycin, was given intramuscularly four times daily in a dose of 12.5 mg. per kilogram, with a maximum dose of 3 gm. daily in adults. At the end of the five days this dose was reduced to 25 mg. per kilogram in children and 2 gm. daily in adults, and if the drug was needed after the 10th day, the adult dose was lowered to 1 gm. daily. Streptomycin was always discontinued by the 15th day."

In the penicillin group there were 2 deaths and 6 neurological complications, and in the penicillin-streptomycin group 5 deaths and 6 neurological complications. No difference between the 2 groups was noted in the rate of return of the spinal fluid to normal or in the subsidence of fever. The death rate was somewhat, but not significantly, higher under the age of 6 months and over 50 years. The last 23 patients were treated alternately with and without hydrocortisone as an additional medicament, with 1 death in each of these 2 groups. No beneficial effect from the employment of steroids could be proved. [It would therefore appear from this experiment that massive systemic penicillin gives rather better results in pneumococcal meningitis than combinations of penicillin with streptomycin and with steroids.] *H. Stanley Banks*

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

DRYL, L. & CYWICKI, J. Dziecieca epidemia duru brzusznego w jednym z powiatów województwa wrocławskiego. [**A Typhoid Epidemic among Children in a District of the Province of Wroclaw**] *Przegląd Epidemiol.* Warsaw. 1959, v. 13, No. 2, 139–47, 3 figs. [11 refs.] English summary (9 lines).

An epidemic of typhoid fever occurred in a district of the Wrocław province of Poland in the summer of 1954. The outbreak lasted from July to the middle of August and 136 cases were recorded; the area was mainly agricultural, with a low population density, and in the preceding 3 years 16, 15 and 25 cases had occurred respectively. Children were mainly affected, 32 cases (23·0%) occurring in children aged up to 5 years, 63 (47·0%) in the 6–10 and 17 (13·0%) in the 11–15 year age-group. In a search for the source of infection, drinking water, milk, ice-cream and river water could be excluded. 88% of the patients were found to have drunk mineral waters obtained from the same factory, in which very insanitary conditions prevailed. In laboratory experiments it was shown that *Salmonella typhi* would survive for up to 3 days at room temperature in beer and soda water produced in the factory, and it was therefore considered likely that the epidemic was due to the consumption of contaminated mineral water, although attempts to detect typhoid carriers among the staff were unsuccessful.

D. J. Bauer

DE LA CRUZ, E. Epidemiología de la salmonelosis en Costa Rica. III. Salmonelas en manipuladores de carnes procesadas. [**Epidemiology of *Salmonella* Infections in Costa Rica. III. *Salmonella* Infections in Handlers of Processed Meat**] *Rev. Biologia Trop.* San José, Costa Rica. 1959, July, v. 7, No. 1, 1–6. [15 refs.]

The English summary appended to the paper is as follows:—

"The incidence of *Salmonella* was studied in employees of the Municipal Slaughterhouse of San José, Costa Rica, and of meat processing plants in the same

community. Twenty per cent of the first group and 18 per cent of the second were found to be carriers. The serotypes of *Salmonella* found are given; of these *S. lomita* and *S. thompson* are reported for Costa Rica for the first time. One individual was found to carry three serotypes (*S. typhi-murium* + *S. lomita* + *S. london*) and two other carriers had two serotypes each (*S. typhi-murium* + *S. london* in one case, *S. bredeney* + *S. eastbourne* in the other)."

KUBINYI, L. A veszprémi és parádsasvári ivóvíz által terjesztett enteritis járványok tanulságai. [**Epidemics due to Drinking Water in Veszprém and Parádsasvár**] *Egészségtudomány*. Budapest. 1959, v. 3, No. 4, 343–50, 2 figs. German summary.

The following is a translation of the German summary:—

The author describes 2 water-borne epidemics of enteritis due to *Escherichia coli* 0–124.

In Veszprém the epidemic involved 30% of the population. The protected area of a group of wells was not enclosed and near the wells was an opening by which water could contaminate the wells. The public health department repeatedly called attention to the risk which this flaw in the protected area entailed, but the defect was remedied only after the epidemic.

In Parádsasvár 56% of the inmates of a children's convalescent home and 20% of the workmen in a glass factory were ill as a result of using infected mineral water. Near the mineral water spring a sewage channel had been constructed without permission.

The organisms could be cultivated from most of the patients, from the well in Veszprém, and from the sewage. These epidemics demonstrate the importance of careful inspection and technical control in the supervision of waterworks and mineral-water establishments. It is essential to make proper arrangements for protected areas and their enclosure.

In most epidemics of intestinal infections attributable to drinking water the organism cannot be identified. The establishment of the role of *E. coli* 0–124 as the pathogen will probably facilitate the investigation of epidemics of enteritis. *Charles Wilcocks*

BUONOMINI, G. & MICHELI, F. Osservazioni sulla brucellosi-infortunio in Toscana. [**Remarks on Occupational Brucellosis in Tuscany**] *Med. d. Lavoro*. 1959, Oct., v. 50, No. 10, 574–92, 7 figs. [10 refs.] English summary.

The authors (the senior of whom is the Director of the Institute of Hygiene of Pisa University) point out first that insurance legislation in Italy recognizes that brucellosis may be a hazard of work, and as such compensatable, and in this paper they report the results of investigating 1,041 cases notified to the various branches of INAIL (National Industrial Insurance Institute) in the administrative region of Tuscany between 1949 and 1957. 789 were from Pisa province alone, 157 from Florence province, and the balance from the other 7 provinces. The low incidence in the other provinces is attributed to ignorance of the law on the part of both doctors and insured and not to absence of the disease.

In Pisa and Florence provinces, especially the former, whole families engaged in farming are liable to contract the disease, but 75% of the incidence was in males mainly between 20 and 50 years of age, and there is a definite seasonal incidence, in the spring. The causative organism is almost always *Br. melitensis* for bovine as well as ovine or caprine infections.

In 75% of patients the incubation period was not more than 68 days with a minimum of 7–8 and a maximum of 7 months. No difference was noted in the incubation periods from the animal infected whether bovine or ovine. 51·29% of the persons contracted the disease after assisting at a bovine parturition or abortion; ovine infections occurred usually after dealing with dung or attending the infected flock. In 50% the disease lasted for more than 4 months and in some for more than 2 years. The minimum duration was 20 days. Treatment was by vaccines, antibiotics, or both combined. Treatment by vaccine alone stopped after 1953, but neither antibiotic treatment by itself nor when combined with vaccine seemed to have shortened the duration of the disease. From the point of view of compensation, in Pisa province 30% of the claims were rejected, though delay in notification, which was as much as 2 years in a few cases, did not appear to be the reason. 84% of the remainder were compensated for temporary incapacity, but *no less than 19% remained permanently incapacitated*. The authors therefore rightly emphasize the very great socio-economic importance of the disease affecting as it does males mostly, in the prime of life, with a long illness and permanently incapacitating 1 in 5.

They consider that in Tuscany the hazard of brucellosis is particularly high; that an increase in the numbers can be expected when the standard of notification in the other provinces reaches that of Pisa; and that in many cases there is a considerable time-lag between the commencement of the disease and notification. In the last 2 years (1955–57) the incidence of the disease among agricultural workers has been especially high.

They recommend particular attention to the campaign against brucellosis in bovines and education of the agricultural population, reduction of the time limits for notification of the disease and improvement in completing the requisite forms. *W. K. Dunscombe*

FUKADA, M. & KITAMURA, S. **Pathology of Human Tularemia in Japan.** *Fukushima J. Med. Sci.* 1958, Dec., v. 5, Nos. 3/4, 113–39, 24 figs. on 6 pls. [37 refs.]

MATVEEV, K. I. & SERGEEVA, T. I. **Peacetime Epidemiology of Tetanus in the U.S.S.R. and Foreign Countries.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 170–80, 1 fig. [12 refs.]

This paper on the problem of tetanus in peacetime is based on "official statistics and literature published

over the last 8–10 years". The disease is first considered as it occurs in the Soviet Union where no official statistics were available before 1948. Since that year the introduction of compulsory notification has been followed by an increase in the apparent incidence. There is an analysis of the figures of incidence in relation to districts of the Soviet Union, and to occupational groups with tables which give also the age distribution and the routes of infection. There is some discussion of the value of active and passive immunization.

Tetanus mortality in other countries is next considered with tables which give total deaths from tetanus and mortality rates for the period 1945–1953 in Western Europe, North and South America, Asia and Oceania and Africa. In the conclusions there is some stress on the need for obtaining better records of incidence in some countries and of the importance of compulsory immunization of all children and certain workers such as "collective farm workers" in areas of high incidence of tetanus.

"During the last 8–10 years the incidence of tetanus and the mortality in foreign countries has been at a high level. In the capitalist countries of Europe, America, Asia and Africa more than 115,000 have died from tetanus and about 350,000 have developed the disease". [The total of deaths from tetanus in the Soviet Union is not stated.] *M. E. Delafield*

MITOW, A. & JANKOW, N. Leptospirenerkrankungen in Bulgarien. [**The Incidence of Leptospirosis in Bulgaria**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 437–44.

[A review of the incidence of leptospirosis in man and domestic animals in Bulgaria was recently published by MATEEW [this *Bulletin*, 1959, v. 34, 1112]. The present article covers much the same ground, but also contains very valuable information about the serological relationships of a variety of "new" serotypes mentioned in that article. This summary therefore can probably most profitably be devoted to a description of these findings.]

Leptospira zalapitza [presumably the same as *L. tzalapitza* mentioned by MATEEW, *loc. cit.*] is identical with *L. pomona.*

L. cotschevo is identical with *L. bataviae.*

L. plovdiv is identical with *L. mini.*

L. nicolaevo belongs to the Autumnalis serogroup but is not identical with either of the 2 subtypes of *L. autumnalis.* [It was not apparently compared with *L. bangkinang.*]

Strain "Warna I" belongs to the Hyos serogroup. The strain was agglutinated to full titre by an antiserum for *L. diva* [which therefore presumably also belongs to that serogroup, but no information is given about its origin or serological relationships].

Strain "Warna II" belongs to the Icterohaemorrhagiae serogroup. *J. C. Broom*

NASSAU, E. & LEVI, E. [**An Epidemic of Listeriosis in Infants in Israel**] *Dapim Refuiim.* Tel Aviv. 1959, Oct., v. 18, No. 4, 187–91. [In Hebrew.] English summary p. 1.

This is a short note on 5 cases of infection with *Listeria* [*Erysipelothrix*] *monocytogenes* in infants, 3 had meningitis. 1 developed sepsis and 1 had meningitis and pneumonia. 2 died. Monocytosis was a feature.

Bacteriological diagnosis rests on recognition of the characteristic Gram-positive diphtheroid organisms, which should not be regarded as harmless contaminants when found in the cerebrospinal fluid. *Charles Wilcocks*

HEDBERG, K., MAGNUSSON, P. H. & NAGLO, O. Ett par fall av listerios. [**Two Cases of Listeriosis**] *Opuscula Med.* Stockholm. 1959, Dec., v. 4, No. 10, 365–72, 4 figs.

The English summary appended to the paper is as follows:—

"In this article two cases of infection with *Listeria Monocytogenes* in newborn or premature infants are reported. The cases were diagnosed in February and March 1959. The first case was a boy, born five weeks before full time. Five hours after birth the child became cyanotic and later on it also got petechial haemorrhages and icterus. Yellow spinal fluid was obtained and Listeria monocytogenes was isolated from this. The diagnosis was verified by inoculation in rabbit eye and mouse peritoneum. In spite of treatment with antibiotics the child died. The autopsy revealed specific granulomas in liver, spleen, lungs, adrenals and brain tissue. The organism was isolated from brain tissue. It belonged to the serological group 1. In serum from the mother antibodies were present in a titer of 1/16 which later rose to 1/32.

"The second case was a girl, born three months before full time. It died during delivery. The autopsy revealed bronchopneumonias in both lungs and haemorrhages in both adrenals. Listeria was isolated from the lung tissue. It belonged to the serological group 4 A. Also in this case serum from the mother showed an antibody titer of 1/16 but unfortunately she has not come for further investigations."

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Enteric group, Arthropod-borne group, Others.*

HUMMELER, K., DAVIDSON, W. L., HENLE, W., LABOCCETTA, A. C. & RUCH, Hilda G. **Encephalomyelitis due to Infection with *Herpesvirus simiae* (Herpes B Virus). A Report of Two Fatal, Laboratory-Acquired Cases.** *New England J. of Med.* 1959, July 9, v. 261, No. 2, 64–8.

The authors have observed 2 fatal cases of B virus infection. (1) An animal-house attendant aged 21, who had been bitten by monkeys on several occasions. 5 weeks after the last bite he developed a febrile illness with convulsions. On examination there was ataxia, a Romberg sign, absence of knee, ankle and abdominal reflexes and unilateral hemianaesthesia. The pressure of the cerebrospinal fluid was 440 mm. of water and

it contained 160 cells per cmm. and 55 mgm.% of protein. Coma and flaccid paralysis developed and death occurred 20 days after the onset of illness. (2) A technician aged 21 who had had no contact with monkeys. On 2 occasions he cut himself with glassware contaminated with fluid from monkey kidney cell cultures. 2 days after the last occasion he developed a febrile illness with blisters at the site of the injury, hyperaesthesia of the affected area and stiffness of the neck. The findings in the cerebrospinal fluid were similar to those in the first case. Muscular weakness and diplopia developed, and death occurred on the 16th day of illness.

In both cases the diagnosis was confirmed by laboratory investigations. [See also this *Bulletin*, 1958, v. 33, 1025; 1959, v. 34, 507.] *D. J. Bauer*

ROGERS, K. D. & GEZON, H. M. **Asian Influenza in High School Students.** *Pub. Health Rep.* Wash. 1959, Oct., v. 74, No. 10, 925–35, 5 figs.

During the 1957 Asian influenza epidemic, in a study of high school pupils in Allegheny County, Pennsylvania, the signs and symptoms reported most commonly with illness (sensitivity) were combined with the signs and symptoms most frequently present in patients showing changes in titre of specific antibody (specificity), to form a sensitivity-specificity index, from which there was constructed a characteristic clinical syndrome for this epidemic. In the corresponding period (Sept.–Oct.) of 1958, when no isolations of influenza virus were made locally and only 5% of the population suffered from the strict influenza syndrome, no such index existed. During the 1957 epidemic, however, the index was so clear-cut that the method is thought to be applicable to epidemics of other specific infections. By means of a sensitivity-specificity index obtained during the early stages of such epidemics, a clinical syndrome might be constructed which could be applied to estimate the incidence of the disease in the later stages of the epidemic, and in this way the need for further laboratory studies might be minimized.

H. Stanley Banks

DUNN, F. L., CAREY, D. E., COHEN, A. & MARTIN, J. D. **Epidemiologic Studies of Asian Influenza in a Lousiana Parish.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 351–71, 7 figs. [15 refs.]

STRÖM, J. **A Comparison between Family Infections during Epidemics of Poliomyelitis and Hepatitis in Stockholm.** *Acta Med. Scandinavica.* 1959, Sept. 30, v. 165, No. 1, 49–54, 2 figs. [11 refs.]

In the epidemiology of poliomyelitis and of epidemic hepatitis there are many similarities but also marked differences. A comparison is made here of the incidence of family infections in the two diseases, as judged during an epidemic year in Stockholm for hepatitis (348 hospital patients in 1949) and for poliomyelitis (962 paralytic and non-paralytic hospital patients in 1953). Compared with persons living on their own, families were attacked much more often by poliomyelitis, but multiple cases in the affected families were far more numerous in the hepatitis epidemic (28·2%) than in the poliomyelitis epidemic (8·6%). In poliomyelitis 90% of the secondary cases appeared within 12 days after the primary case, and were therefore probably infected from some common intensely infective source about the same time as the primary case. The remaining 10% of secondary cases in poliomyelitis came in 3 waves at an interval of about 8–15 days (the usual incubation period of poliomyelitis). In hepatitis the curve of secondary cases was quite different, about 50% of them occurring in two main groups about 30 and 60 days respectively after the primary cases. In hepatitis, therefore, contact infection within the family from the primary case, or from secondary cases, is a significant factor. It is because of these secondary family infections that gamma globulin prophylaxis is so useful in hepatitis, and comparatively useless in poliomyelitis.

In both these diseases in Stockholm there has been a considerable shift towards infection of higher age-groups. This probably reflects the impaired immunity of adults to both infections, owing to the reduced infection among young children associated with rising standards of hygiene. *H. Stanley Banks*

CELERS, J., DROUHET, V., SAÏD, G. & SOULÉ, J. L. Études immunologiques sur la poliomyélite. IV. Dépistage des anticorps neutralisant les trois virus poliomyélitiques chez quelques étudiants parisiens. Confrontation des résultats sérologiques et de certains éléments du mode de vie. [**Neutralizing Antibodies for the Three Poliomyelitis Viruses in Parisian Students; Relationship to Social Factors**] *Rev. d'Immunologie.* 1959, July–Sept., v. 23, No. 4, 299–311.

A serological survey for poliovirus neutralizing antibodies among 144 university students in Paris is reported. The sample was not truly representative containing more females and foreigners than the student population. Antibodies were very prevalent, 40% having them to all 3 types and only 2% lacking antibodies to any type. Antibodies to each individual type were present in about 3/4 of the individuals. Extensive analysis of various social and economic factors which have been found elsewhere to effect the acquisition of antibodies are presented. In this selected population the chief factors appeared to be age and instability (*i.e.* households with a variable population) of the family group, increase in both of these favouring acquisition of antibodies. *A. J. Beale*

DUMITRESCU, V., POPESCU, G., MOROIANU, S. B. & SGÎNDĂR, P. Considerații epidemiologice asupra evoluției poliomielitei în Romînia înainte de introducerea vaccinării antipoliomielitice (1927–1957). [**The Epidemiology of Poliomyelitis in Rumania before the Introduction of Immunization (1927–57)**] *Studii si Cercetări Inframicrobiol.* 1959, v. 10, No. 2, 119–42, 7 figs. French summary.

[This abstract is taken from the French summary.]

The authors show that in Rumania poliomyelitis has been continuously extending in the period reviewed,

with epidemic outbreaks of increasing extent. It is widespread in rural areas, and the frequency of severe forms of the disease has increased; family foci of multiple cases have become more numerous. In inter-epidemic periods the towns have provided the reserve of virus.

Poliomyelitis has remained a disease of the early years of life, but recently the incidence has changed, and the disease is found in infants under 1 year (or even 6 months), and also in adolescents and adults. This change has taken place at the same time as the spread of the disease into rural areas where the people, owing to the rarity of previous epidemics, are relatively non-immune.

In all epidemics Type 1 virus has been predominant, and recently the Coxsackie viruses have frequently been encountered.

At the present time, thanks to the large-scale introduction of free immunization in 1957, the epidemiological picture has completely changed, and fewer cases are now reported. *Charles Wilcocks*

Saïd, G., Drouhet, V., Soulé, J. L. & Celers, J. Étude des anticorps neutralisant les virus de la poliomyélite chez trois groupes d'enfants africains de la région de Dakar. [**Study of Neutralizing Antibodies to Poliovirus in 3 Groups of African Children in the Dakar Region**] *Bull. Soc. Méd. Afrique Noire Langue Française.* Dakar. 1959, v. 4, No. 2, 145–55, 1 map & 5 figs. [12 refs.]

The results of a serological study for antibodies to the 3 types of poliovirus on 366 children, of whom 160 were less than 3 years and 90 less than 1 year, in French West Africa is described. 217 of the children lived in Dakar, 98 in Popenguine, a fishing village south of Dakar, and 51 in an agricultural village inland. In all 3 areas it was found that the acquisition of all 3 types of antibody was very rapid and similar to the findings elsewhere in Africa, *e.g.* by Melnick and others [this *Bulletin*, 1952, v. 27, 1092 *bis*] in Egypt. The lowest incidence of antibodies was reached at about 1 year and thereafter antibodies were rapidly acquired so that nearly 100% of the individuals had antibodies to all 3 types by 4 years of age. There was very little difference in the rate of acquisition of antibodies in the 3 areas. *A. J. Beale*

Sureau, P. La poliomyelite à Madagascar. [**Poliomyelitis in Madagascar**] *Arch. Inst. Pasteur de Madagascar.* 1959, v. 27, 37–45.

An account of cases of poliomyelitis in Madagascar is reported together with more recent virus studies. Poliomyelitis in Madagascar is a rare sporadic disease of infants amongst the native population. Poliovirus antibodies of all 3 types are acquired very early in life, thus 43% of a small sample of infants 0–4 years had all 3 types and 97% at least 1 type. In 1958, 7 poliovirus isolations were made from paralysed patients and 1 from a contact. 3 were type 1 and 5 type 2. It is noted that by contrast with the native population adult visitors from countries enjoying a higher hygienic standard are much more prone to contract paralytic poliomyelitis. *A. J. Beale*

Dougherty, W. J. & Faro, S. N. **Factors affecting the Incidence and Severity of Poliomyelitis. An Analysis of the 1958 Epidemic in New Jersey.** *New England J. of Med.* 1959, Nov. 5, v. 261, No. 19, 934–6.

The epidemicity of poliomyelitis during the last half century has been very variable from year to year. In New Jersey the year 1958 was one in which the incidence was greatly increased over that of the previous 2 years; 266 cases were reported and 8 deaths. Attention was thus focused on the incompleteness of the poliomyelitis immunization carried out in the area; the unerring ability of an infectious agent to seek out susceptible persons was clearly demonstrated.

Only 16% of pre-school children had been triply vaccinated, and the unvaccinated children under 5 years bore the brunt of the attack, 35% of the paralysed patients being in this age-group. Less than 10% of the paralytic patients had received a complete course of Salk vaccine. Moderate to severe residual disability occurred in over 50% of the unvaccinated paralysed patients, and the degree of disability did not appear to be related to the type of virus isolated. Approximately 80% of paralytic cases were proved by virus isolation. The attack rates for non-whites were 5 times that for the white population. The epidemic emphasized the need for a scheme of immunization covering the community more effectively. *H. Stanley Banks*

Semple, A. B., Parry, W. H. & Griffith, A. **The Occurrence of Sensitivity Reactions to Poliomyelitis Vaccine in Liverpool.** *Med. Officer.* 1959, Nov. 20, v. 102, No. 21, 261–3. [16 refs.]

Between January and July 1959, 42,644 poliovaccine injections were given at the health clinic in Liverpool. During this time 70 examples of vasomotor symptoms following vaccination were noted. 22 were judged to be emotional reactions and 48 allergic manifestations probably due to the trace amounts of penicillin in the vaccine. As a result the subjects were asked about previous sensitivity reactions before vaccination, and if there was such a history 0·1 ml. of poliovaccine was given intradermally. 19 out of 22 gave a positive reaction. 100 mgm. of anthisan was given 20 minutes before vaccination in sensitive subjects. It is said that with this routine 20 out of 22 people failed to show a reaction to vaccination.

[In a table giving details of these 22 persons, 21 appeared to have had antihistamine premedication, some only before the 2nd injection. 2 of these had reactions after anthisan, but there were several who had reactions after injection without antihistamine protection.]

1 of those who did have a severe reaction to a first dose also had a mild reaction to a second dose, with Connaught Laboratories vaccine which does not contain penicillin. It is concluded from this experience that other components of the vaccine can probably cause sensitivity reactions. *A. J. Beale*

THOMPSON, R. Q., THOMPSON, C. & PUGH, C. T. **A Method for Detection and Estimation of Penicillin in Poliomyelitis Vaccine.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 377–80, 1 fig.

"A method is described for determining penicillin in poliomyelitis vaccine. This method consists of acidifying the vaccine, extracting the penicillin into diethyl ether, removal of ether by vacuum distillation and transfer of penicillin into a buffer. The penicillin is determined by standard paper chromatographic and bioautographic technics. This method is capable of detecting 0·001 unit of penicillin/ml finished vaccine."

GILLETT, R. L. **Acute Benign Pericarditis and the Coxsackie Viruses.** *New England J. of Med.* 1959, Oct. 22, v. 261, No. 17, 838–43, 2 figs. [13 refs.]

15 cases of acute benign pericarditis, associated with evidence of coxsackie virus infection, have been reported in the last few years, and earlier there were reports of an association between pericarditis and pleurodynia. 4 new cases are now reported in which appreciable levels of antibody to coxsackie virus group B and type 5 were demonstrated (with a 4-fold rise of titre in 2) coincident with clinical, radiographic, and electrocardiographic evidence of acute benign pericarditis; in 2 of these cases this virus was isolated from the stools. The patients were young adult male naval personnel.

Of the total 19 cases thus reported, coxsackie virus Group B type 5 was implicated in 16, Group B type 3 in 2, and Group A type 1, in 1. The antibody results might have been more decisive if in all cases the first serum sample had been taken early in the illness. The disease seems to clear satisfactorily with bed rest, but in 2 of the 4 new cases the pericardial friction rub persisted for about 10 weeks from onset.

H. Stanley Banks

NULL, F. C., Jr. & CASTLE, C. H. **Adult Pericarditis and Myocarditis due to Coxsackie Virus Group B, Type 5.** *New England J. of Med.* 1959, Nov. 5, v. 261, No. 19, 937–42, 8 figs. [39 refs.]

A number of diverse human illnesses have now been shown to be associated with the Coxsackie viruses. In the spring and summer of 1957 an epidemic of infections due to Coxsackie virus Group B type 5 occurred in Salt Lake City; among 17 of the patients, in all of whom this virus was incriminated by virus isolation from stools or pharynx or by serology, 11 had pleurodynia, 1 aseptic meningitis, 1 meningoencephalitis, and 4 had pericarditis, of whom 2 showed signs of myocarditis in addition. This article describes fully 3 of these cases, all in young adults. There were signs of moderate or slight pericarditis, and electrocardiographs showed T-wave inversion in leads 1, 2, aVL, aVF, and V_2–V_6; both of these conditions cleared up in about 6 weeks. The myocarditis in 2 of these cases included severe cardiac decompensation in 1. Coxsackie myocarditis has previously been reported in infants, but this is believed to be the first known instance in adults. The condition cleared satisfactorily in these cases within 6 to 7 months, but the prognosis in viral myocarditis generally should be guarded. *H. Stanley Banks*

NEVA, F. A. & MALONE, Mary F. **Persistence of Antibodies to ECHO-16 Viruses following Boston Exanthem Disease.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 233–5.

Sera from 15 patients who had suffered from Boston exanthem in 1951 or 1954 [this *Bulletin*, 1956, v. 31, 1065] were tested for neutralizing and complement-fixing antibody at various times up to 6 years after infection with the aetiological virus (ECHO 16). It was found that there was very little change in neutralizing antibody titre. All the changes that did occur were in one family. It is possible that high neutralizing antibody titres were maintained in part by infections with other enteroviruses. Complement-fixing antibody titres fell about 2–4-fold in the first year but thereafter remained stationary. All the sera from an individual patient were tested simultaneously.

A. J. Beale

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE. **Viral Hepatitis. Clinical and Public Health Aspects** [EICHENWALD, H. F. & MOSLEY, J. W.]. *Pub. Health Service Publication No. 435* (Revised 1959). pp. iv + 56, 5 figs. [32 refs.] Wash. 25, D.C.: Superintendent of Documents, U.S. Govt. Printing Office. [$0.20.]

This is a useful, low-priced, booklet in which the clinical and public health aspects of viral hepatitis are reviewed in a practical workmanlike manner. It has been written to help general practitioners, hospital medical officers, health officers, and other public health workers who want information on the generally accepted methods for the diagnosis, treatment, and prevention of hepatitis. More specialized aspects of the subject, such as pathology and the complex chemistry of liver disease, are covered only in outline, and the references are not listed (though a list of additional reading is given). The booklet is meant to be a practical guide rather than a scholarly treatise, and as such it is to be highly commended.

The distinction between infectious and "serum" hepatitis is now sharpened into that between virus A and virus B disease; and the differences between the two are well defined in respect of: (a) route of infection, (b) site in which the virus can be demonstrated, (c) incubation period, (d) usual type of onset, (e) hepatic function tests, (f) prophylaxis by immune globulin (applies only to virus A), and immunity after infection (no cross-immunity has been demonstrated). These differences are fully discussed and are held to justify this sharp classification into two distinct diseases [which is not yet generally adopted in Britain, although the differences are admitted]. The treatment and complications, and also congenital hepatitis (virus B only) are dealt with briefly but adequately for the purpose. The sections on epidemiology and control of virus A,

use of immune globulin, and epidemiology and control of virus B (which includes a full discussion of "syringe hepatitis") are particularly useful.

The second part of the booklet outlines the role of health departments in relation to epidemiology and 5 useful appendices set out practical procedures.

H. Stanley Banks

MOSLEY, J. W. **Water-Borne Infectious Hepatitis.** *New England J. of Med.* 1959, Oct. 1 & 8, v. 261, Nos. 14 & 15, 703–8; 748–53, 2 figs. [59 refs.]

This is a review of the 28 epidemics of infectious hepatitis attributed in the literature to drinking contaminated water. 6 of them occurred in towns of over 3,000 population served by a municipal supply, 5 were in villages, and 1 in a rural area; the remaining 16 involved groups exposed to private water supplies in institutions, industrial plants, or summer hotels or camps. This distribution is similar to that seen in outbreaks of gastro-enteritis, diarrhoea, dysentery, and typhoid in the United States during the period 1938–45. The seasonal incidence of infectious hepatitis was much the same in these epidemics as that of endemic hepatitis, that is November to June, except that the largest number of cases occurring in any one month was in August. In 3 of the epidemics, analysis of the time pattern of occurrence of the cases showed it to be consistent with an incubation period of the disease between 22 and 46 days.

The attack rates for icteric cases in epidemics involving a defined population group exposed during a limited time to a heavily contaminated private supply, varied from 12 to 44%, most being around 30%. These rates are comparable to those seen after experimental infection in human volunteers. The age-specific attack rates in 3 of the largest water-borne epidemics are analysed, and adults, especially the younger adults, were found to be principally attacked, compared with children in endemic hepatitis. This would doubtless reflect the age groupings of those principally exposed to the infection under the 2 different sets of conditions and, at least in part, the severity of their reactions to it.

Experimental studies have shown that the virus of infectious hepatitis is resistant in raw water to residual chlorine of 1 p.p.m. for 30 minutes; it is probably one of the hardiest of the pathogenic micro-organisms in respect of survival in water. It seems surprising that water-borne infection in this disease has not been more often reported. Further data should be available once the possibility of water-borne infection is more widely realized.

H. Stanley Banks

KRUGMAN, S., WARD, R., GILES, Joan P., BODANSKY, O. & JACOBS, A. M. **Infectious Hepatitis. Detection of Virus during the Incubation Period and in Clinically Inapparent Infection.** *New England J. of Med.* 1959, Oct. 8, v. 261, No. 15, 729–34, 4 figs. [12 refs.]

Since 1953 some 500 cases of infectious hepatitis have been observed in an institution for mentally defective children in New York. Since most of the newly admitted children would certainly acquire the disease, it was considered justifiable, with parental consent, to inoculate batches of them with serum containing the local virus in order to study the natural history and period of infectivity of the disease. In fact the inoculated disease proved on the whole to be milder than the natural disease. Virus was detected in stools and blood during the incubation period and early in the course of the disease; stools were also shown to be infective on the 25th day of the incubation period (or 2–3 weeks *before* the onset of jaundice) and also 1–8 days after the onset of jaundice but not later. These observations confirm and extend the findings of earlier authors [PAUL *et al.*, this *Bulletin*, 1946, v. 21, 11; HAVENS, *ibid.*, 489].

The presence of virus in blood and stools 2–3 weeks before the onset of jaundice has profound public health implications. Viraemia was also detected in an asymptomatic patient—an inoculated subject who had, as the sole evidence of anicteric disease, an increase in serum transaminase activity after an incubation period of 37 days. The detection of viraemia in a case of inapparent hepatitis confirms the suspicion, based on much epidemiological evidence, that the numerous persons with subclinical disease are probably active and efficient disseminators of the virus. *H. Stanley Banks*

DOWNS, W. G., AITKEN, T. H. G. & SPENCE, L. **Eastern Equine Encephalitis Virus isolated from *Culex nigripalpus* in Trinidad.** *Science.* 1959, Nov. 27, v. 130, 1471.

In May 1959, 512 *Culex nigripalpus* (many engorged) caught in chicken-baited traps near Sangre Grande were inoculated into 2-day-old mice. The first mouse died after 5 days and passage from the brain of a sick mouse resulted in isolation of a virus killing adult and suckling mice in 2 days. Re-isolation was successful. Neutralization tests with immune and hyperimmune sera to eastern equine encephalitis virus showed the virus isolated to be identical or closely related. 2 further strains were isolated from pools of 249 and 142 *Culex* (*Melanoconion*) *taeniopus* trapped in August and September. Both were re-isolated. The first strain was isolated when bird migration was northward and the others when migration was southward.

C. E. Gordon Smith

JUBA, A. Klinisches Bild und Histopathologie der im Komitat Békés beobachteten Zeckenenzephalitis. **[Clinical Picture and Histopathology of Tick-Borne Encephalitis observed in Békés County]** *Acta Med.* Budapest. 1959, v. 14, No. 1, 33–49, 8 figs. [34 refs.]

An account is given of 18 serologically confirmed cases of tick-borne encephalitis which occurred between 1950 and 1955 in the area of Békés in Hungary. The meningo-encephalitic form of the disease was observed in 2, poliomyelitic in 3, meningeal in 5 and the influenzal form in 3 cases. Details of the clinical findings are given in a table. 2 cases were fatal. Histological examination of the brains revealed infiltration and

haemorrhages in the meninges, infiltration in layers 3–5 of the cortex with neuronophagia, and extensive destruction of Purkinje cells. *D. J. Bauer*

WOODALL, J. P. & BERTRAM, D. S. **The Transmission of Semliki Forest Virus by *Aëdes aegypti* L.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, Nov., v. 53, No. 6, 440–44.

A strain of *Aëdes aegypti* originating from West Africa and colonized since 1926 was used. Mosquitoes were infected by feeding on week-old mice inoculated 24 hours previously with Semliki Forest virus. Mosquitoes fed on mice infected with 116th mouse-passage virus were fed in batches of 1–5 on baby mice. Transmission occurred from the second until the 46th day after feeding of the mosquitoes. Mosquitoes fed on mice infected with 7th mouse-passage virus successfully transmitted to 3 of 5 baby mice 24 hours later. The heads and salivary glands of these mosquitoes were immediately afterwards ground up and inoculated into mice—virus was found in the heads, but not the salivary glands. With 7th passage virus, mosquitoes were allowed to feed partially on a viraemic mouse and partially on a normal mouse and transmission occurred to 2 of 3 of the latter. The authors believe that biological transmission occurs from as early as the 48th hour after an infective feed as they found virus in the salivary glands at that time. *C. E. Gordon Smith*

KOKERNOT, R. H. & MCINTOSH, B. M. **Isolation of West Nile Virus from a naturally infected Human Being and from a Bird, *Sylvietta rufescens* (Vieillot).** *South African Med. J.* 1959, Nov. 21, v. 33, No. 47, 987–9.

An African trapping birds in Tongaland, South Africa [this *Bulletin*, 1958, v. 33, 561], had a mild one-day fever. Blood obtained while he was febrile was inoculated into 1-day-old mice all of which were dead or sick after 4 days. Second passage material was pathogenic for adult mice. Re-isolation was achieved. Sera of the patient obtained in the acute phase and 5 weeks later revealed a significant increase of neutralizing antibody to the virus isolated. A rise in haemagglutinin-inhibiting antibody (10 to 640) was also found and 7 months after the infection the titre had fallen to 80. Cross-neutralization tests with West Nile virus showed the virus isolated to be identical or closely related.

A similar strain of virus was isolated from the liver and spleen of a crombec warbler (*Sylvietta rufescens*) trapped where the patient had been working.

[See also this *Bulletin*, 1958, v. 33, 1001; 1959, v. 34, 421.] *C. E. Gordon Smith*

ALBAGALI, C. & CHAIMOFF, R. **[A Case of West Nile (W.N.F.) Myocarditis)]** *Harefuah.* Jerusalem. 1959, Nov. 15, v. 57, No. 10 [in Hebrew 274–5, 1 fig. (21 refs.) English summary 275–6].

The English summary appended to the paper is as follows:—

"Myocarditis following virus infections has repeatedly been reported in the literature.

"We observed a patient with all the clinical signs of diffuse myocardial damage while suffering from West-Nile-Fever.

"The patient, a 30-year-old male, claimed to have always been healthy. He suffered from a 4 days' fever, headache, anorexia, palpitations, some stabbing sensation and pressure in his left chest. While the pyrexia subsided rapidly, palpitations and chest discomfort persisted for a considerably longer period. Complement fixation which was initially negative for WNF rose to 1/480, 70 days after the onset of illness, and dropped later to 1/160. This serological sequence is diagnostic for WNF.

"Electrocardiographic changes, such as diffuse "T" wave changes, temporary auricular fibrillation and numerous premature contractions together with the clinical course, justified in our opinion the diagnosis of myocarditis as a complication of WNF.

"As far as we are aware, this is the first published case of myocarditis in connection with WNF. In view of the fact that this virus disease is endemic in Israel, the importance of possible cardiac complications is being stressed. Routine electrocardiographic examinations with parallel virological investigation in patients suspected of suffering from WNF may help to classify more cases of myocarditis whose etiology has so far remained undetermined."

DOHERTY, R. L., CARLEY, J. G. & LEE, Patricia E. **Studies of Arthropod-Borne Virus Infections in Queensland. I. A Serological Survey of Aboriginal Missions bordering the Gulf of Carpentaria.** *Australian J. Exper. Biol. & Med. Sci.* 1959, Aug., v. 37, Pt. 4, 365–72, 1 fig. [18 refs.]

267 sera were collected from aborigines at Missions or towns in Queensland bordering the Gulf of Carpentaria. They were tested in neutralization tests in mice against 100 LD50 of Murray Valley encephalitis, dengue-1, dengue-2, Japanese encephalitis and West Nile viruses. They were also tested for haemagglutinin-inhibiting antibodies against Murray Valley virus. All groups of aborigines tested except 1 had evidence of Murray Valley infection, the incidence of antibody being about 80%, except in 2 places where it was less. The sera from 1 Mission were analysed by age-group: 0 of 15 children aged 2–3 years had antibody, but 4 of 9 aged 4 had neutralizing antibody and most of the older age-groups had incidences as high or higher, the maximum being 20 of 26 aged 11–15. Of the 267 sera there were only 20 which did not neutralize Murray Valley virus, but did neutralize one or more of the other viruses. 5 of these in 1 group neutralized dengue-1, dengue-2 or both and presumably indicated past dengue infections.

In the haemagglutinin-inhibition tests kaolin was not found sufficiently reliable for absorption of non-specific inhibitors and acetone extraction was used. Results of haemagglutinin-inhibition and neutralization tests agreed in 80% of the sera tested; 44 sera had neutralizing

antibody only and 14 haemagglutinin-inhibiting antibody only.

Sera from 11 fowls introduced to the area in 1957 had no antibodies, but 6 of 7 introduced in 1953 did have antibody. Antibodies were also demonstrated in wallabies (6/6), wild ducks (1/5) and in 1 galah.

Murray Valley infections appear to have been widespread on the Gulf of Carpentaria. The age-incidence of antibodies in children and fowls suggest that the last activity of the virus in this area was in 1954 or early 1955. *C. E. Gordon Smith*

BLISS, C. I. & BLEVINS, D. L. **The Analysis of Seasonal Variation in Measles.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 328–34, 2 figs.

The logarithms of the attack rates of measles among children aged under 15 years in old Baltimore during the 31 years 1901–1931 have been examined by harmonic analysis by using a 2-term Fourier curve. During the period the annual epidemic of measles underwent several changes, the peak incidence varied between January and May and the minimum incidence between August and October, the 2-year cycle of large outbreaks which have been broadly the pattern of the disease was broken by 2 successive low or large outbreaks and the epidemic year was changed from the odd to the even-dated year. The analysis of variance of the components of the equation shows that the general form of the measles curve for the 31 years can be described by a 2-term Fourier curve but that the annual curves showed significant variations from this pattern. *W. J. Martin*

GRIMMER, H. & JOSEPH, A. **An Epidemic of Infectious Erythema in Germany.** *Arch. Dermat.* 1959, Sept., v. 80, No. 3, 283–5.

This is a short paper describing probably the most extensive epidemic of erythema infectiosum (fifth disease) yet reported. In contrast to most previous outbreaks (in children's institutions) this was a true city-wide explosive epidemic, with a morbidity estimated at 50,000 cases in Berlin alone; it occurred in October–November 1958 and abated after a period of about 4 weeks. Similar outbreaks had occurred previously in Kiel, Hamburg, Münster, Bremen, and especially in Osnabrück. As is usual in extensive epidemics of the exanthemata, the rash was well marked and its incidence high. This report is based on 200 cases treated within a month in a skin clinic in Berlin.

In this material there were more than twice as many women as men, adolescents and the middle-aged being in the majority; children were decidedly in the minority, although it was ascertained that the attack rate in the nurseries and schools throughout the city ranged from a few isolated cases to some 20%. Familial infection was noted only in 10% of the cases; the evidence was therefore in favour of widespread infection with many in the population apparently immune. No virological studies were made, but the outbreak is attributed to a mutated virus. Features suggestive of an allergic element obtruding in the post-acute stage were a marked eosinophilia (up to 34%) and the oral and genital mucosal lesions mentioned below; in the early acute stage there was a leucocytosis with a shift to the left.

The incubation period is said to have varied from 5 days to 2 weeks (but in the latter instances there may have been a missed intervening case). Onset was sudden, with few and minor prodromata before the rash appeared on hands, arms, and face, and spread to the trunk and lower extremities including the soles. The rash varied greatly in appearance, especially at the height of the epidemic—from morbilliform on face and limbs to large bright red patches covering the greater part of the body and sometimes becoming haemorrhagic, or accompanied by oedema; in some cases there were patches of urticaria and even vesicles. Most patients had mild general symptoms only, but in severe cases there was moderate to high fever, rheumatic pains, and circulatory disturbances. The mucous membrane of the mouth showed sharply outlined dark red spots, and occasionally small ulcers, and the genitalia were similarly affected—balanitis and vaginitis with pruritus and discharge. The conjunctivae were inflamed in a few instances. The rash cleared after 4–20 days and an occasional relapse was seen. *H. Stanley Banks*

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

LIDWELL, O. M., NOBLE, W. C. & DOLPHIN, G. W. **The Use of Radiation to estimate the Numbers of Micro-Organisms in Air-Borne Particles.** *J. Hygiene.* 1959, Sept., v. 57, No. 3, 299–308, 1 fig.

The size-grading sampler recently described by Lidwell [this *Bulletin*, 1959, v. 34, 921] separates an airborne cloud of bacteria-carrying particles into 4 categories, according to the size of the particle. The present paper describes a method for enumerating the viable bacteria in the particles of different sizes. The culture plates exposed in the size-grading sampler were exposed to a high-intensity electron beam in a linear accelerator, sections of the plates being given different doses. From the position and slope of the line on a graph relating the count on the sections of the plate to the dose, it was then possible to determine the mean number of viable units per clump.

Results are presented for airborne salivary particles dispersed by a "spraying spit" and for *Staphylococcus aureus*-containing particles from hospital air; the mean numbers of viable units per particle in the 4 particle size ranges were:—

	Salivary organisms	*Staph. aureus*
$>18\mu$	11·0	6·0
$10–18\mu$	8·9	4·2
$4–10\mu$	4·7	3·0
$<4\mu$	2·4	*ca* 1·0

R. E. O. Williams

ROTHSTEIN, A. **Role of the Cell Membrane in the Metabolism of Inorganic Electrolytes by Microorganisms.** *Bact. Reviews.* 1959, Dec., v. 23, No. 4, 175–201, 16 figs. [126 refs.]

TUFFERY, A. A. **The Health of Laboratory Mice. A Comparison of General Health in Two Breeding Units where Different Systems are employed.** *J. Hygiene.* 1959, Dec., v. 57, No. 4, 386–402, 5 figs. [12 refs.]

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Colicines; Other Therapeutic Substances; Disinfection.**

KNUDSEN, E. T. & ROLINSON, G. N. **Absorption and Excretion Studies of the Potassium Salt of 6 (α - Phenoxypropionamido) Penicillanic Acid.** *Lancet.* 1959, Dec. 19, 1105–9, 6 figs.

This paper by members of the staff of Beecham Research Laboratories describes experiments with a new form of penicillin for oral administration recently marketed under the name Broxil, but referred to here as BRL152. This and penicillin V were given in single 250 mgm. doses to 10 fasting normal subjects and the antibiotic was assayed in the blood after 1, 2, 4 and 6 hours. Individual and mean concentrations found are given in Tables, and means are also represented graphically. The peak concentrations attained by BRL152 exceeded those of penicillin V by 2-fold or more, and those of the former remained higher up to the 4th hour; the assayable level at the 6th hour was so often *nil* with both drugs that findings for this period seem to have little significance. 2 such experiments were done, with similar results, the drugs being given in one in solutions and in the other as tablets. Urine was collected for 6 hours after the dose in male subjects: the percentages of the dose excreted were 64 and 60% of BRL152, and 50 and 40% of penicillin V. [This is a greater excretion of penicillin V than has previously been found—*e.g.*, by HEATLEY (this *Bulletin*, 1956, v. 31, 936), and does not seem consistent with the difference in blood levels.] A 500 mgm. tablet was given to 5 of the subjects who had previously been given a tablet of 250 mgm. and the serum concentrations are described as being doubled [actually they are greater by factors of 2·6, 3·2, and 3·3 at 1, 2 and 4 hours, an improbable result which may only indicate a disadvantage of depending in such studies on small numbers of subjects]. A comparison was also made between the serum concentrations produced by a 250 mgm. tablet of BRL152 and an intramuscular injection

of 400,000 units of sodium penicillin, somewhat to the advantage of the former, since this shows a slower fall after a similar peak level. *L. P. Garrod*

STROMINGER, J. L., PARK, J. T. & THOMPSON, R. E. **Composition of the Cell Wall of *Staphylococcus aureus*: its relation to the Mechanism of Action of Penicillin.** *J. Biol. Chem.* 1959, Dec., v. 234, No. 12, 3263–8, 3 figs. [51 refs.]

SCIPLE, G. W., KNOX, J. M. & MONTGOMERY, C. H. **Incidence of Penicillin Reactions after an Antihistaminic simultaneously administered parenterally.** *New England J. of Med.* 1959, Nov. 26, v. 261, No. 22, 1123–5. [17 refs.]

"In a controlled study of a series of 4537 patients, an antihistaminic was administered simultaneously with penicillin to determine if the incidence of penicillin reactions could thereby be reduced. Benzathine penicillin, procaine penicillin with 2 per cent aluminium monostearate in oil and chlorprophenpyridamine maleate injected intramuscularly were the agents used.

"Chlorprophenpyridamine maleate in 10 mg. and 20 mg. doses injected intramuscularly with penicillin did not decrease the incidence of voluntarily reported penicillin reactions as compared to the control group."

LOGUE, J. T. & BARRETT, J. T. **Repeated Nonfatal Anaphylactic Shock from Intramuscular Penicillin.** *Antibiotic Med.* New York. 1959, Nov., v. 6, No. 11, 672–4. [13 refs.]

CITRI, N. & GARBER, N. **The Effect of Urea on the Activity of Penicillinase.** Reprinted from *Biochim. et Biophys. Acta.* 1958, v. 30, 664–5, 2 figs.

MIYASHITA, Y. **Biochemical Studies on Streptomycin-Resistant Tubercle Bacilli. Effects of Streptomycin on Nucleic Acid fractionated by Ecteola-Cellulose.** *Nagoya J. Med. Sci.* 1959, Nov., v. 22, No. 3, 267–81, 13 figs. [48 refs.]

KUNIN, C. M., DORNBUSH, A. C. & FINLAND, M. **Distribution and Excretion of Four Tetracycline Analogues in Normal Young Men.** *J. Clin. Investigation.* 1959, Nov., v. 38, No. 11, 1950–63, 6 figs. [42 refs.]

A single intravenous injection of 500 mgm. tetracycline (TC), 500 mgm. oxytetracycline (OTC), 500 mgm. chlortetracycline (CTC) or 250 or 500 mgm. demethylchlortetracycline (DMCT) was given to 4 healthy young men: each was given each antibiotic, at an interval of 1–2 weeks. Assays were carried out on blood collected at intervals ranging from 30 minutes to 30 hours after the injection, and on 24-hour specimens of urine collected during the 3 succeeding days.

The findings are analysed and presented in 7 different ways. Concentrations found in the blood during the middle and latter part of the 30-hour period of observation were highest after 500 mgm. DMCT, lowest after CTC and intermediate after TC, OTC and 250 mgm. DMCT. The "half-life" of each antibiotic in hours was CTC 5·6, TC 8·5, OTC 9·2 and DMCT 11·8 (250 mgm. dose) or 12·7 (500 mgm.). "Relative distribution volumes" were calculated and found to be highest for OTC, indicating greater sequestration in the liver or elsewhere. Among rates of clearance for serum that of CTC was highest, and much the most rapid renal clearance was that of OTC. Urinary recoveries were OTC 70%, TC 60, DMCT 42 and CTC 18. "Non-renal removal" was 3–4% per hour for each antibiotic except CTC, which was more rapid owing to its instability. Percentages bound to plasma were found in separate equilibrium dialysis experiments to be CTC 47, DMCT 41, TC24 and OTC 20.

The paper concludes by pointing out that although all these assay results are absolute values (*i.e.* determined against a standard of the same antibiotic) a truer picture of therapeutic activity is obtained by expressing them as equivalents of a single standard such as TC. [This is disputable. Fig. 6, showing average serum levels as TC equivalents, represents relative activity only against the assay organism used. This was *Bacillus cereus*, infection with which does not exist. Had a pathogenic organism been used, the picture would have been similar, but because such comparisons are valid only for one species, there is much to be said for determining actual w/v concentrations: these can always be interpreted in the light of any known difference in activity among the tetracyclines against a particular organism.] *L. P. Garrod*

LAMPEN, J. O., MORGAN, E. R., SLOCUM, Adelaide & ARNOW, P. **Absorption of Nystatin by Micro-organisms.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 282–9, 3 figs. [21 refs.]

Nystatin dissolved in a solution of dimethylsulphoxide was added to suspensions of various micro-organisms. After maintenance at 30°C. for various periods (30 minutes in most of the tests) the mixture was chilled and centrifuged, and the antibiotic was estimated in the supernatant by a spectrophotometric method. It was thus shown that sensitive species (*Saccharomyces cerevisiae, Candida albicans*) absorbed substantial quantities, calculated to amount to as much as 0·6% of the dry cell weight, whereas insensitive organisms (*Streptomyces* spp. and 2 bacteria) absorbed little or none. A more resistant strain of *C. albicans* absorbed less than a sensitive one (but the differences shown in Table 1 are small). The higher the concentration of the antibiotic the greater was the amount absorbed.

Absorption was also accelerated by increase in temperature up to 55°C., and by a reduction in *p*H; it did not occur in the absence of an energy source. The somewhat different conditions governing absorption by heat-killed yeast cells were also studied, and conclusions are drawn about the mechanism of absorption by living cells. *L. P. Garrod*

ROTHENBERG, H. J. **Anaphylactoid Reaction of Vancomycin.** *J. Amer. Med. Ass.* 1959, Oct. 24, v. 171, No. 8, 1101–2.

A girl of 17 with an old rheumatic history and mitral insufficiency developed signs of an acute endocarditis following a minor skin lesion and while doing part-time work in hospital. This was assumed to be due to a penicillin-resistant staphylococcus (subsequently confirmed: no mention of sensitivities to other antibiotics) and without awaiting the results of 6 blood cultures done at 2-hour intervals, she was given 1 gm. vancomycin in 250 ml. 5% dextrose intravenously. The infusion occupied 25 minutes: 10 minutes after its completion "she suddenly developed chest pain, dyspnoea, generalized pruritus, urticaria on her arms, back and chest, and swelling of her face, lips and eyelids". She was also cyanosed and had a barely perceptible radial pulse. She was revived with adrenaline and oxygen and later given an anti-histamine. "Therapy was then changed" [to what and with what result is not recorded]. She was not an asthmatic or known to be allergic to anything except that a sulphonamide had produced a rash 4 years before. This is said to be the first record of such a reaction to vancomycin.

L. P. Garrod

PULASKI, E. J. & TUBBS, R. S. **Inhibitory Effects of Kanamycin and Diffusion into Various Body Fluids.** *Antibiotic Med.* New York. 1959, Oct., v. 6, No. 10, 589–93, 1 fig. [11 refs.]

Kanamycin was compared with neomycin in its capacity to inhibit the growth of 50 strains of *Staphylococcus aureus* and 6 strains each of 5 species of Gram-negative bacilli, rather to the advantage of neomycin (results are only given as numbers of strains inhibited by each of 6 and 8 concentrations respectively).

Kanamycin was assayed in various fluids of patients given it by intramuscular injection, comparison being made with levels in the blood. None was found in cerebrospinal fluid or amniotic fluid. Concentrations in bile were low, in cord blood (inexplicably) variable, in pleural fluid low, and in synovial fluid remarkably high, in 2/5 estimations equal to that in the blood.

L. P. Garrod

KURYŁO-BOROWSKA, Zofia. **Isolation and Properties of Pure Edeine, an Antibiotic of the Strain** *Bacillus brevis Vm4. Bull. Inst. Marine Med. Gdańsk.* 1959, v. 10, Nos. 3/4, 151–63, 8 figs. [16 refs.]

This paper describes an examination of the physical and chemical properties of edeine, an antibiotic produced by *Bacillus brevis*, strain Vm 4. An acid hydrolysate was shown to contain arginine, glycine, glutamic acid, tyrosine and other amino acids not yet identified. The author claims to have shown that edeine differs from other known antibiotics produced by this species. No information is given which has any bearing on the possible practical usefulness of this discovery.

L. P. Garrod

VINCENT, J. G., VEOMETT, R. C. & RILEY, R. F. **Antibacterial Activity associated with** *Lactobacillus acidophilus. J. Bacteriology.* 1959, Oct., v. 78, No. 4, 477–84, 1 fig. [23 refs.]

There is some previous evidence that intestinal lactobacilli produce a substance antagonistic to other bacteria, particularly coliform bacilli. This substance may contribute to maintaining the normal balance among the faecal flora, and may be of importance in connexion with superinfections during antibiotic therapy and with post-irradiation bacteriaemia.

These authors have extracted a substance having antibacterial activity from strains of *Lactobacillus acidophilus* from the faeces of 5 animal species: the most active strains were from rabbits, the least active from mice, the source of the others being man, rat and hamster. It could not be obtained from cultures in liquid media: the production medium used was "liver veal agar plus an additional 0·5 per cent of agar", which was "seeded throughout" and incubated for a varying number of weeks. The method of extraction from this and 2 methods of assay are described. Efforts at purification produced instability and inactivity in serum-containing medium. No hint of the possible chemical structure of "lactocidin", as the substance is called, is given. Activity is expressed in units: much of the material used apparently had an activity of only 0·5–2 units per mgm. The sensitivity to it of 27 species of bacteria and 4 of fungi was determined. The most sensitive were *Proteus*, *Salmonella*, *Pasteurella*, *Escherichia* and *Pseudomonas* spp. (killed by 1–2 units per ml.). Gram-positive species were rather more resistant, but *L. acidophilus* itself was killed by 5 units per ml. [Antibiotics do not destroy the organisms forming them. This observation seems to throw considerable doubt on the nature of the substance.]

L. P. Garrod

BRUMFITT, W. **The Mechanism of Development of Resistance to Lysozyme by some Gram-Positive Bacteria and its Results.** *Brit. J. Exper. Path.* 1959, Oct., v. 40, No. 5, 441–51, 7 figs. (1 on pl.). [34 refs.]

Micrococcus lysodeikticus was rendered highly resistant to egg-white lysozyme. Cell walls from these resistant organisms and from the original sensitive culture were submitted to detailed chemical examination. The only difference found was in the O-acetyl content: this was *nil* in the sensitive culture and 2·9% by weight in the resistant. That this is the change on which resistance depends was shown by treatment of resistant cells with weak alkali; this restored sensitivity, whereas sensitive cells O-acetylated with acetic anhydride became resistant. *Bacillus megaterium* and *Streptococcus faecalis* were also habituated to lysozyme and the same chemical change was demonstrated in their cell walls. *Staphylococcus aureus*, found to have a 2·0% O-acetyl content in the cell wall, remained totally lysozyme-resistant after de-acetylation: its resistance must therefore have some other explanation.

L. P. Garrod

DONOVAN, J. W., LASKOWSKI, M., Jr. & SCHERAGA, H. A. **Carboxyl Group Interactions in Lysozyme.** [Correspondence.] *J. Molecular Biol.* London. 1959, Sept., v. 1, No. 3, 293–6, 2 figs.

WALLACH, D. P. & THOMAS, R. C. **Psicofuranine. VIII. Some Pharmacological Observations.** *Antibiotics & Chemotherapy.* New York. 1959, Dec., v. 9, No. 12, 722–9.

DYTRYCH, O. Chemická kontrola povrchové dezinfekce. —I. [**Chemical Control of Surface Disinfection. I.**] *Československ. Hyg.* Prague. 1959, v. 4, No. 6, 350–55. English summary (9 lines).

The author has developed a method for detecting chlorine and formaldehyde on the surfaces of objects which have been subjected to disinfection. A swab moistened with water is rubbed over the surface of the treated object and then extracted with 3 cc. of water. For the detection of chlorine the solution thus obtained is treated with 3–4 drops of a 1:10 dilution of a 1% solution of ortho-tolidine in concentrated hydrochloric acid. Free chlorine produces a yellow colour; the method is suitable for controlling disinfection with chloramine, calcium hypochlorite and other substances which liberate chlorine. For the detection of formaldehyde the solution is mixed with 2 cc. of a 0·1% aqueous solution of phloroglucin and a few drops of 12% sodium hydroxide solution are added. A red colour develops in the presence of formaldehyde.

The quantitative estimation of chlorine and formaldehyde by standard chemical methods is also described in detail. *D. J. Bauer*

STEEL, K. J. **A Note on the Reaction of Mercuric Chloride with Bacterial -SH Groups.** *J. Pharmacy & Pharmacol.* London. 1960, Jan., v. 12, No 1, 59–61, 1 fig.

"A linear relation is obtained when the logarithm of the number of organisms (*E. coli*) in inocula is plotted against the logarithm of the quantity of mercuric chloride theoretically necessary to produce bacteriostasis, expressed as a percentage of that practically required. No direct relation exists between the number of organisms and the amount of mercuric chloride necessary to produce bacteriostasis. Mercuric chloride is non-specific in its reaction with bacterial sulphydryl groups. Cells of *E. coli* contain about 10^8-SH groups per cell."

AYLIFFE, G. A. J., ALDER, V. G. & GILLESPIE, W. A. **The Disinfection of Bath Water with Hexachlorophane.** *Lancet.* 1959, Sept. 26, 456–8, 3 figs.

A 1 in 50,000 solution of hexachlorophane (the substance known in the U.S.A. as hexachlorophene) was found to kill staphylococci rapidly: Gram-negative bacilli were more resistant to a variable degree. This concentration was attained in a bath by adding 1 oz. (28 ml.) of a 10% solution (the substance being dissolved in spirit and alkali) to a 30 gallon bath occupied by a bather: enumeration of the bacteria in the water before and after showed a steep fall following the addition, and swabs from empty baths so used gave much reduced bacterial growths with almost complete absence of *Staphylococcus aureus*. Among patients taking 4,000 baths with this addition only 3 complained of slight skin irritation. The authors acknowledge that baths can be adequately disinfected with hypochlorite and a detergent, as described by BOYCOTT [this *Bulletin*, 1957, v. 32, 175] but this relatively laborious process is apt to be omitted at busy times, whereas tipping the whole contents of a small bottle into the bath involves no trouble. *L. P. Garrod*

MERIVALE, W. H. H. **The Contribution of Laundering to Hygiene.** *J. Roy. Inst. Pub. Health & Hyg.* 1959, Dec., v. 22, No. 12, 282–90. [36 refs.]

This is the printed version of a lecture given at the Royal Institute of Public Health and Hygiene and largely consistent of a review of the danger of cross-infection in hospitals, the special problems of contaminated fabrics and the methods available for their disinfection. It is emphasized that while the processes commonly used to launder cotton goods can be expected to yield a virtually sterile product, this is not true of blankets, which are normally washed at lower temperatures and lower degrees of alkalinity. Various methods recently described for incorporating disinfectant in the washing process are discussed, as are methods in which higher temperatures are used. It is concluded that a number of satisfactory processes exist which can render blankets safe.

The author also reports his experiments with roller towels of the continuous strip pattern, housed in a special cabinet and laundered commercially. He found that although used rolls were heavily contaminated they were almost completely sterilized in the washing process. Preliminary experiments are reported in which a marker organism was used to investigate whether the unused, clean part of the roll could be contaminated by the used, dirty part. No contamination was demonstrated. The author describes experiments in which dry cleaning was found to be effective for disinfecting blankets. He also showed that if formalin is included in the dry-cleaning process the blankets will acquire germicidal properties which are retained for at least a week.

This article is a most helpful introduction to the whole subject and contains a useful list of references. *J. C. Kelsey*

KING EDWARD'S HOSPITAL FUND FOR LONDON. **Division of Hospital Facilities. An Interim Report on the Cleansing and Sterilization of Hospital Blankets.** 59 pp. 1959, Nov. London: 34, King Street, E.C.2. [2s.]

In recent years there has been much interest in this subject and many papers have been published. King

Edward's Fund are to be congratulated on this attempt to bring together the available information in a single pamphlet. This is in two parts. In the first the present position is summarized under 12 headings, ranging from a short paragraph to over a page in length. These headings include types of blanket, warmth, dust and fluff, shrinkage, inflammability, colour, cost, cleansing and sterilization, and recontamination. A brief introduction outlines the field of enquiry and a final section reaches some rather tentative conclusions, the main one being that there are several possible solutions to the problem and that only experience will show their relative merits. The second and greater part of the pamphlet consists of brief abstracts of published papers and reports, arranged under the same 12 headings as the first part.

This is only an interim report and in the introduction originality and finality are specifically disclaimed, but it is a most useful and timely publication and a goldmine of information and references. It should be consulted by all who are concerned with the hospital blanket. *J. C. Kelsey*

PRESSLEY, T. A. **Comparison of Various Hospital Blankets after Repeated Laundering.** *Med. J. Australia.* 1959, Nov. 14, v. 2, No. 20, 721–3, 1 fig.

"Laboratory and laundry tests of a wide variety of blankets suggest that cotton terry towelling and shrink-resistant all-wool blankets have a long life under conditions of frequent washing. Blankets of both types have been washed and tumble-dried over two hundred times and are still in a serviceable condition. The colour of the shrink-resistant wool blankets deteriorated when the Blowers and Wallace laundering technique was employed and the domestic Melbourne water supply containing iron compounds was used, but this discoloration can be avoided by modification of the laundry method."

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

VASSILIADIS, P. & MAQUET, R. Comportement des Staphylocoques dans le milieu au cyanure de potassium. **[Behaviour of Staphylococci in a Potassium Cyanide Medium]** *C.R. Soc. Biol.* 1959, v. 153, No. 5, 871–2.

In a fluid medium containing 1/53,200 potassium cyanide, all of 42 strains of coagulase-positive staphylococci grew well in 48 hours (36 in 24 hours) compared with only 7 of 33 coagulase-negative strains. It was found necessary to replace the cotton-wool plug of the tube with waxed cork. *R. E. O. Williams*

ALAMI, S. Y. & KELLY, F. C. **Demonstration of Staphylococcal Clumping Factor and Free Coagulase in Soft Agar Media.** *J. Bacteriology.* 1959, Oct., v. 78, No. 4, 539–44, 2 figs. [14 refs.]

Tubes of nutrient broth containing 0·15% or 0·3% agar, 1% human plasma and 0·4% fibrinogen were inoculated with dilutions of staphylococcal cultures to give 20–40 colonies. After incubation, strains producing free coagulase were surrounded by a zone of coagulation in the medium; those producing bound coagulase had compact colonies; those producing neither had diffuse colonies. Strains producing both coagulases showed a compact colony within a coagulation zone. There was almost complete correlation of the results in the plasma-fibrinogen-soft-agar medium with those obtained by conventional tests. *R. E. O. Williams*

WLODARCZAK, K. & JELJASZEWICZ, J. **Influence of Coagulase on the Growth of Staphylococci in Normal Human Serum.** [Correspondence.] *Nature.* 1959, Nov. 7, v. 184, Suppl. No. 19, 1514–15. [12 refs.]

Coagulase-positive staphylococci generally grow readily in fresh human serum whereas coagulase-negative strains do not. Addition of coagulase-containing culture filtrate to the serum was found to promote the growth of coagulase-negative strains, but addition of purified coagulase had no such effect.
R. E. O. Williams

YOTIS, W. W. & EKSTEDT, R. D. **Studies on Staphylococci. I. Effect of Serum and Coagulase on the Metabolism of Coagulase Positive and Coagulase Negative Strains.** *J. Bacteriology.* 1959, Oct., v. 78, No. 4, 567–74, 6 figs. [10 refs.]

Conventional manometric techniques were employed to show that coagulase positive strains of *Staph. aureus* respired in human serum much more actively than did coagulase negative strains. Glucose, pyruvate and brain heart infusion broth were oxidized equally well irrespective of coagulase activity. Differences in nutritional requirements or permeability of the 2 groups of organisms did not seem to be implicated in the oxidation of the human serum. The addition of purified coagulase stimulated the respiration in human serum of both coagulase positive and coagulase negative strains. The negative strains were stimulated about twice as much as the positive strains.
H. Gooder

GRÜN, L. Die serologische Differenzierung von Staphylokokken. [**The Serological Typing of Staphylococci**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 146, No. 2, 129–41. [Numerous refs.]

Pursuing his investigations of the agglutination typing method for staphylococci devised by OEDING, Grün has found that the agglutinations are more easily carried out in well-plates incubated in a moist chamber for 2 hours at 37°C. He also found that the most suitable cultures for the test are those grown at 40°C. for 5 hours; this temperature is definitely preferred to 37°C. With 9 sera staphylococci can be classified, first, into 5 principal groups on the basis of their reactions with the factor sera *a*, *b*, *c*, and *e*; and these groups can be further subdivided with the sera *h*, *i*, *k*, *l*; serum *d* is species-specific. Various experiments are quoted to support the view that the agglutination typing method gives reproducible results; and the large number of types recognized conforms with the results obtained with phage typing. Nevertheless, in the final discussion Grün concludes that the difficulties and work demanded for the preparation and use of typing sera are hardly justified by the uses to which the results can be put and he thinks that simpler methods, such as determinations of the antibiogram or lipase activity will ordinarily suffice. [In the reviewer's experience the antibiogram is often a quite unreliable method for unravelling the details of staphylococcal epidemics.]

R. E. O. Williams

HOEPRICH, P. D. & WHITESIDES, J. N. **Grid Branded Disposable Petri Dishes for Bacteriophage Typing of Staphylococci.** *Amer. J. Clin. Path.* 1959, Nov., v. 32, No. 5, 495–7, 2 figs. [Reprinted from *Tech. Bull. Registry Med. Technol.* 1959, Oct., v. 29, No. 10, 177–9.]

The authors describe a metal grid which is placed on an electric hotplate and used for branding a pattern of 25 squares on to plastic Petri dishes containing media. This method is inexpensive and plates so branded are suitable for bacteriophage typing of staphylococci. [Marked plates are not necessary when the phages are applied by some mechanical means.]

M. Patricia Jevons

MENOLASINO, N. J. **Tetrazolium Chloride as an Indicator in Bacteriophage Typing of Staphylococci.** *Amer. J. Clin. Path.* 1959, Dec., v. 32, No. 6, 578–9. [Reprinted from *Tech. Bull. Registry Med. Technol.* 1959, Nov., v. 29, No. 11, 192–3.]

"The 2,3,5-triphenyl-tetrazolium chloride added to the tryptone-soy agar resulted in a contrast between the staphylococcal growth and areas of phage lysis which, compared to control plates that did not contain the tetrazolium, was a distinct advantage in reading the results of typing with phage. The method is simple, efficient, and economical."

RUYS, A. Charlotte & BORST, J. **A New Method of the Reporting of Phage Patterns of** *Staphylococcus aureus*. *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 2, 237–40, 1 fig.

In reporting the results of phage typing of staphylococci it has been customary to list the phages producing strong lysis and to add a "+" sign, if additional weaker reactions were noted. The present authors suggest that it would be better to report, in order of "conspicuity", all the reactions observed, separating by "/" signs the reference numbers of the phages producing different degrees of lysis. This enables the recipient of the report to appreciate the resemblances between different strains more than is possible with conventional reports and has been found valuable in epidemiological studies. [Many will, however, feel that the reporting of phage types is already sufficiently complex to be daunting, and that for ordinary routine work, the interpretation of the results may be better done in the typing laboratory.] *R. E. O. Williams*

SCHÖNFELD, J. K., with the technical assistance of H. A. DE HAAS-POPPINGA. **"L" Forms of Staphylococci; their Reversibility; Changes in the Sensitivity Pattern after Several Intermediary Passages in the "L" Phase.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 3, 325–31, 2 figs.

Penicillin-sensitive staphylococci gave rise to unstable L forms when plated on solid media containing 3% salt and 100 units/ml. penicillin [previously described by DIENES and SHARP, this *Bulletin*, 1957, v. 32, 601]. Reversion to the coccal form occurred on transfer to penicillin-free media or by the action of penicillinase applied to the surface of a medium containing fully developed L colonies. The original phage typing patterns of the staphylococci were maintained through as many as 25 consecutive passages in the L form. Naturally occurring staphylococci resistant respectively to chloramphenicol and tetracycline were found to have lost this resistance after reversion to the coccal form following less than 10 consecutive passages in the L phase. Strains rendered resistant in the laboratory to tyrothricin and streptomycin remained resistant after 20 passages as L forms. The authors feel that the loss of antibiotic resistance in the L phase is not due to mutation [though the evidence presented does not rule out this possibility]. *H. Gooder*

ROGERS, H. J. & PERKINS, H. R. **Cell-Wall Mucopeptides of** *Staphylococcus aureus* **and** *Micrococcus lysodeikticus*. *Nature.* 1959, Aug. 15, v. 184, 520–24, 2 figs. [32 refs.]

Recent observations related to concepts about the structure and biosynthesis of the cell walls of, in particular, staphylococci and micrococci are discussed. Evidence is presented which points toward a possible heterogeneity of the cell wall mucopeptides in these organisms. Structural observations on the complex fragments of cell walls of *M. lysodeikticus* obtained by either acid hydrolysis or lysozyme action suggest that the lysozyme labile bond is scattered through the molecules of the polymer or polymers rather than occurring at frequent regular intervals. Studies on the incorporation of glycine into staphylococcal mucopeptides, in

which crushed organisms were used, revealed that the small number of whole cells remaining in such a preparation had a greatly increased synthesizing activity per cell compared with the original suspension.

H. Gooder

BERGDOLL, M. S.; SUGIYAMA, H.; DACK, G. M.; HIBNICK, H. E. **Staphylococcal Enterotoxin. I. Purification** [BERGDOLL, SUGIYAMA & DACK]. *Arch. Biochemistry.* 1959, Nov., v. 85, No. 1, 62–9, 2 figs. [19 refs.] **II. Chemistry** [HIBNICK & BERGDOLL]. *Ibid.*, 70–73, 1 fig. [10 refs.]

(i) "A procedure for purifying enterotoxin from the *Staphylococcus* strain S-6 has been outlined. Acid precipitation, adsorption on alumina, precipitation by ethanol, chromatography on IRC-50, and zone electrophoresis on starch were the methods used. The final product shows the presence of only one antigen when tested by the gel-diffusion technique of Oakley and only one peak in the ultracentrifuge. A preparation was obtained that causes emesis in monkeys at approximately 1 μg. nitrogen per dose."

(ii) "A study of some chemical and physical properties of purified staphylococcal enterotoxin has been reported. The enterotoxin has a molecular weight of 24,000 ± 3000 and an isoelectric point at pH 8.6. There is no indication of the presence of carbohydrate and lipide. The amino acid content has been determined."

PILLET, J., ORTA, B. & PERRIER, M. Immunisation du lapin en deux injections par l'anatoxine staphyloccique alpha. Influence de l' intervalle, de la dose et de la voie d'introduction de l'antigène. [**Immunization of Rabbits by Means of Two Injections of Staphylococcal α-Toxoid. Influence of the Interval, of the Dose, and of the Route of Inoculation**] *Ann. Inst. Pasteur.* 1959, Sept., v. 97, No. 3, 353–9.

In tests of variations in the method of immunizing rabbits with staphylococcus α-toxoid, it was found necessary, for reproducible results, to use only animals having an initial titre of α-antitoxin of 0·04 units/ml. or less. There was no difference in the titre reached after intravenous, intradermal, or subcutaneous injection though the last seemed to give the most rapid response. The final titre increased with an increase in the interval between the 2 doses, up to an optimum at about 14–20 days. In experiments in which either 1st or 2nd dose was held constant at 10 units, it was found that the optimum 2nd or 1st dose respectively was also about 10 units. *R. E. O. Williams*

COHN, Z. A. & MORSE, S. I. **Interactions between Rabbit Polymorphonuclear Leucocytes and Staphylococci.** *J. Exper. Med.* 1959, Sept. 1, v. 110, No. 3, 419–43, 7 charts. [37 refs.]

Polymorph leucocytes from peritoneal exudate of rabbits were tested for their ability to phagocytose various strains of staphylococci. The 2 ml. test mixture contained about 30×10^6 leucocytes per ml. and 20–60×10^6 bacteria per ml., with 10% rabbit serum. The tubes were agitated during incubation at 37·5°C. At intervals up to 3 hours the viable bacteria were enumerated, the "total" count being made after homogenization to destroy the leucocytes; separate counts were also made of the bacteria in the supernatant and the sediment after spinning.

In the presence of normal rabbit serum, coagulase-negative staphylococci were rapidly ingested by the leucocytes and the total viable count fell about 1,000-fold in 3 hours; at this time all the viable cocci were associated with the leucocytes. Since the "sediment" count did not increase when the "supernatant" count decreased, it was clear that the ingested cocci must be killed rapidly.

Under the same circumstances, there was hardly any evidence of phagocytosis of a coagulase-positive staphylococcus from the viable counts; examination of stained films showed some ingestion, which was increased if the ratio of bacteria to leucocytes was increased. On the other hand 4 species of Gram-negative bacilli were ingested and killed. *Mycobacterium smegmatis* appeared to be ingested but not killed by the leucocytes.

When a specific antiserum was included instead of normal serum, the coagulase-positive staphylococci were ingested and killed in the same way as the coagulase-negative. The serum was active in a dilution of 1:640 but apparently required complement. The antiserum was also able to cause agglutination of the cocci and in cross-absorption experiments removal of the agglutinating antibody also removed the opsonizing effect.

R. E. O. Williams

WARREN, G. H. & GRAY, Jane. **Isolation and Purification of Streptococcal Hyaluronic Acid.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 125–7, 2 figs. [14 refs.]

"1. Hyaluronic acid was released from cells of a Group A *Streptococcus pyogenes* when the latter was grown in medium in which all constituents except casein hydrolysate were chemically defined. With this medium it has been posible to produce high yields of streptococcal hyaluronic acid following 16 to 18 hour incubation at 37°C. 2. Stability of hyaluronic acid in growing cultures of *S. pyogenes* following addition of a hyaluronidase inhibitor, alginic acid sulfate, to the medium, together with a significant increase in hyaluronic acid levels of the broths is further evidence that strains of streptococci which produce hyaluronic acid also produce hyaluronidase. 3. Isolation and partial purification of the bacterial mucopolysaccharide are described."

PALCZUK, N. C. & FLICK, J. A. **Studies on a Skin-Fixing, Reagin Blocking, Antipneumococcal Antibody.** *J. Immunology.* 1959, Oct., v. 83, No. 4, 339–47. [19 refs.]

Serum was obtained from 3 volunteers, 2 of whom were atopic, immunized with a mixture of pneumococcal polysaccharides. These were used to prepare skin

sites in skin sensitive patients in Prausnitz-Küstner tests. Inhibition of wheal and erythema (reagin-antigen) reaction by these sera indicated a blocking effect. Blocking effect in normal subjects could also be demonstrated by preparation of skin sites with a mixture of reaginic serum from a sensitive subject and serum containing blocking factor, and subsequent challenge with antigen.

The skin-fixing blocking factor was heat stable, and apparently specific, it could be demonstrated for up to 15 days in prepared skin sites of sensitive subjects and experiments suggested it was due to an antibody and not to residual polysaccharide in the donor serum. Studies with purified antigen injected into prepared sites suggested that previous experiments had given results due to the composite reaction of several systems.

The blocking factor could not be demonstrated to coprecipitate with immune rabbit serum on addition of antigen, but the human serum contained other antibodies to the polysaccharide fraction used for immunization. *M. Patricia Jevons*

DESBORDES, J., PERCHERON, F., FAYET, Marie T. & BLOMET, J. Contribution à la connaissance des protéines des mycobactéries. [**A Contribution to the Study of Mycobacteria Proteins**] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 35–50, 2 figs. [36 refs.]

IONESCO-MIHĂIEŞTI, C., DÂMBOVICEANU. A. & VAINER, Henriette. Le métabolisme des aminoacides chez les mycobactéries. Asparaginase et transaminases chez les bacilles tuberculeux de type humain H_{37} *Rv* et $H_{37}a$, de type bovin *Vallée*, de type aviaire *Griffith* et de la souche saprophyte *Mycobacterium phlei* 61. [**Amino-Acid Metabolism in Mycobacteria. Asparaginase and Transaminases in Tubercle Bacilli of the Human Type (H_{37} *Rv* and $H_{37}a$) of the Bovine Vallée Type, of the Avian Type (Griffith) and in the Saprophytic Strain** ***Mycobacterium phlei*** **61**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Sept., v. 18, No. 3, 323–45, 20 graphs & 2 figs. [16 refs.]

WINDER, F. **Catalase and Peroxidase in Mycobacteria. Possible Relationship to the Mode of Action of Isoniazid.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 68–78. [46 refs.]

FUKAI, K. & SELLERS, Margret I. **A Morphologic Study of Mycobacteria infected with D32 Phage.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 52–9, 12 figs. on 4 pls.

ANNEAR, D. I. & ANDERSON, K. **The Use of "Hibitane" in the Culture of Sputum for** *Mycobacterium tuberculosis.* *Med. J. Australia.* 1959, Sept. 26, v. 2, No. 13, 444–6.

In this trial 140 specimens of sputum were homogenized by shaking 8 ml. volumes of the specimens with 15 ml. phosphate buffer *p*H 7·0 for 5–10 minutes at 10 strokes per second with an amplitude of 4 inches. 5 ml. of the mixture was then treated with an equal volume of 0·1 N NaOH, shaken at half speed for 2–5 minutes and then neutralized. A second 5 ml. quantity was mixed with 10 ml. of the phosphate buffer, 0·5 ml of Hibitane Concentrate [this *Bulletin*, 1954, v. 29 1095] added and the mixture shaken for 3 minutes (The final concentration of Hibitane was 1:1,500.) Both fractions of each specimen were cultured on Löwenstein slopes.

Of the 140 specimens, 24 were negative and 101 were positive by both methods, and 3 were positive by the alkali method and negative by the Hibitane method; none gave the reverse result. 12 of the specimens treated by the Hibitane method were grossly contaminated but none treated by the alkali method was contaminated to the same degree. However, with 36 specimens the growth of tubercle bacilli was heavier after the Hibitane treatment compared with only 10 specimens in which the growth was heavier after the alkali treatment.

The authors emphasize that this comparison is only exploratory for variations in using the antiseptic were not investigated, and they draw special attention to the fact that satisfactory liquefaction of the sputum can be achieved simply by vigorous shaking.

S. R. M. Bushby

WAYNE, L. G. **Some Observations on the Use of Benzalkonium Chloride (Zephiran) in Tuberculosis Bacteriology.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 912–13.

"Benzalkonium chloride at 0.05 per cent final concentration, when used as a decontaminating agent for specimens to be cultured for tubercle bacilli, may be carried over to agar medium in quantities sufficient to exert some bacteriostatic effect. There is no significant 'carry-over' effect on egg medium.

"Bacilli from resected lesions were just as viable after benzalkonium chloride treatment as were bacilli from untreated control specimens."

PARAF, J., DESBORDES, J., FOURNIER, É. & BLOMET, J. Contribution à l'étude de l'extraction de la tuberculine des cellules d'une mycobactérie pathogène (souche H37Rv). [**Contribution to the Study of the Extraction of Tuberculin from the Cells of Pathogenic Mycobacteria**] *Rev. d'Immunologie.* 1959, July–Sept., v. 23, No. 4, 312–22, 1 chart. [11 refs.]

IMAKI *et al.* (*Japanese J. Tuberculosis*, 1955 v. 3, 80) and ITO (*Amer. Rev. Tuberculosis*, 1953, v. 67, 526) showed that tuberculin could be extracted from tubercle bacilli with sodium citrate.

In the present paper the authors report that extraction of the washed growth of a 26-day-old growth of H37Rv on 50 ml. of Sauton medium, with 20 ml. of 0·1 M sodium citrate *p*H 7·0 for 24 hours at 37°C., yields an extract which, when diluted 1:1,000, gives skin reactions only a little less than those of tuberculin containing 100,000 units/ml. These tests were done in 5 tuberculous patients, and no reactions were obtained if the bacilli were killed by heating at 120°C. before extraction or if the extraction of the living bacilli was made with distilled water or normal saline. The active

trate extract was filtered through a sintered glass ter and sterilized by heating at 100°C. for 1 hour.

Tests made in tuberculous guineapigs showed that xtraction with other salts yielded less active extracts; ne salts used, and in descending order of effectiveness, ere sodium acetate, sodium oxalate, sodium tartrate, odium phosphate, sodium nitrate and sodium chloride. odium chloride at 2·9% yielded extracts that were ightly active, but with 0·8% the extracts were inactive.

The addition of substances that are known to affect ne permeability of cells, *i.e.* 0·01M solutions of mer- uric chloride, zinc sulphate and silver nitrate and the ddition of protoplasmic denaturing agents, *i.e.* 90% cohol, prevented the extraction by sodium citrate.

As this method is similar to that used by RAYNAUD *Ann. Inst. Past.*, 1951, v. 80, 356; 1952, v. 83, 693) or extracting the diphtheria and tetanus toxins, the uthors suggest that there is a relationship between uberculin and these toxins. *S. R. M. Bushby*

OUMANS, G. P. & YOUMANS, Anne S. **The Relationship of Sex to the Susceptibility of Normal and Immunized Mice to Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 750–52.

In 1950 the authors reported [this *Bulletin*, 1952, v. 7, 327] that in experiments with the Strong A strain f mice, the males survived an infection with H37Rv little longer than did the females, but there was no atistical significance between the survival of the 2 exes. In 1957 HOYT *et al.* (*Amer. Rev. Tuberculosis*, 957, v. 75, 618), however, reported that female mice f the Olitsky strain were more susceptible to infection ith H37Rv than were the males. In the present aper the authors are now reporting the results of their xamining data that they have collected from experi- ents with immunized and non-immunized mice con- ucted since their first publication.

All the mice were infected intravenously with 1 mgm. I37Rv and the vaccines were injected intraperitoneally, ne challenge being given 28 days later. From 1952, to 959, 196 male and 217 females mice were vaccinated ith BCG, and 61·7% and 55·3%, respectively, of the groups survived more than 30 days but this differ- nce, by the chi-squared test, is not significant. How- ver, in experiments in which H37Ra was used as the accine, a significant difference was found between the rvival of the sexes, for of 404 vaccinated males 58% rvived over 30 days, as compared with 45·9% of 880 emales ($p = 0·001$); in these experiments there was lso a significant difference ($p = <0·001$) between the rvival times of the unvaccinated control male and emale mice. The difference in survival was also pparent when the analysis was restricted to the 14 xperiments conducted during the shorter period of 958–9; of the vaccinated mice 54% of 261 males as ompared with 42·1% of 202 females survived >30 ays, although the difference in survival of the 2 sexes f the control animals, in which 4·96% of 262 males s compared with 2·91% of 206 females survived over 0 days, was not significant.

The authors therefore conclude that the male mice of ne Strong A strain respond slightly but definitely more effectively to immunization against tubercle bacilli than do the females, and that the females may be slightly more susceptible than the males to tuberculous infection.

S. R. M. Bushby

YOUMANS, G. P., YOUMANS, Anne S. & KANAI, K. **The Difference in Response of Four Strains of Mice to Immunization against Tuberculous Infection.** *Amer. Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 753–6. [Refs. in footnotes.]

The strains of mice used in these experiments were Strong A, Rockland "all purpose", Rockland "specific pathogen-free", and CF; they were vaccinated by intraperitoneal injection and challenged intravenously with 1 mgm. H37Rv. The median survival time of the unvaccinated mice was 13–15 days and no significant difference was observed between the strains. The immunological response to vaccination with BCG or H37Ra was assessed by the percentage of the mice that survived 30 days. The experiments with the 4 strains were not made at the same time but, in the authors' opinion, the highly standardized nature of the infection makes a comparison of the results valid.

The immune response was highest in the CF strain, 98·6% of the male mice surviving 30 days when immunized with BCG. This survival rate compared with 61·7% for the Strong A strain and only 35·7% of the females of the Rockland "all purpose" strain. The superior immunological response of the CF strain was also supported by the results of experiments in which the vaccine was H37Ra, but the response to injection of the "red fraction" extracted from H37Ra after mechanical rupture of the bacilli [this *Bulletin*, 1958, v. 33, 511] was no greater than that given by the Strong A strain. The weakest response was obtained with the Rockland "specific pathogen-free" strain.

In discussing these results the authors stress 2 points; firstly, that attempts to measure the natural resistance of different mouse strains to the tubercle bacilli may merely measure difference in capacity to develop acquired resistance, and secondly, that a strain of mice which shows a high capacity to develop immunity when vaccinated with living tubercle bacilli may not show similar superiority when vaccinated with fractions of the bacilli. *S. R. M. Bushby*

TSUKAMURA, M., NODA, Y., HAYASHI, M. & YAMAMOTO, M. **A Genetic Study of the Cycloserine-Resistance of *Mycobacterium tuberculosis* var. *hominis*.** *Japanese J. Microbiol.* 1959, Jan., v. 3, No. 1, 1–8, 2 figs.

The bacilli used in this study were a clone grown from a single isolate of the Aoyama-B strain of the human tubercle bacillus. Growth from Ogawa medium was shaken with beads and 0·02 ml. of 10-fold dilutions of the suspensions were inoculated onto tubes of this egg medium, containing various concentrations of cycloserine. The average number of colonies that grew on 10 replicate tubes was recorded after 4 weeks' incubation. This procedure was repeated 6 times with the bacilli from the medium containing the highest concentration of the antibiotic on which there was growth; these concentrations were 10, 20, 50, 100, 100 and 200

μgm./ml., respectively, and no further increase in resistance occurred during the last passage.

The average numbers of the colonies growing in the presence of each of the concentrations of cycloserine of each of the 7 passages are presented in tabular and graphical forms, and they show that there are 2 points of discontinuity in the development of resistance. The irregularities can be accounted for by assuming the development of 2 new genotypes, one of which produced the phenotypes resistant to concentrations between 20 and 70 μgm./ml., and the other for those resistant to 70 to 200 μgm./ml. *S. R. M. Bushby*

TSUKAMURA, M., NODA, Y., YAMAMOTO, M. & HAYASHI, M. **Genetic Studies on the 4-Acetylaminobenzaldehyde-Thiosemicarbazone (Tibione) Resistance in** *Mycobacterium tuberculosis* **var.** *hominis. Japanese J. Microbiol.* 1959, Jan., v. 3, No. 1, 17–26.

These investigations on the development of resistance to Tibione were conducted on lines similar to those used for cycloserine [above] the tubercle bacilli used were the clone developed from a single isolate of the Aoyama-B strain.

The number of bacilli that grew in the presence of Tibione was observed to decrease regularly as the concentration of the drug increased from 0 to 50 μgm./ml., except within the range of 0·4 to 0·5 μgm./ml. That the regular decrease in the number of bacilli growing in concentrations of 0 to 0·4 μgm./ml. was due to phenotype variations of the wild sensitive genotype was confirmed by showing that a culture derived from a single bacillus that grew in the presence of 0·3 μgm./ml. behaved in the same way as the parent culture when passaged a second time, and that the bacilli growing in 0·4 μgm./ml. were mutants was shown by the fact that they still retained their resistance after passage through drug-free medium.

The bacilli that grew in the presence of 0·5 μgm./ml. had 2 colonial forms; the majority grew as smooth colonies but a few grew as rough elevated colonies and these were shown to be capable of growing in the presence of 50 μgm./ml.; this difference in colonial form occurred only in the presence of the drug for in its absence all the bacilli grew as rough colonies.

From the results of examining the population structure of 17 single clones from resistant mutants growing in the presence of 1 μgm./ml., the rate of spontaneous appearance of highly resistant mutants in a strain of low resistance, and the population structure of the growth of the bacilli growing in concentrations ranging from 0·3 to 50 μgm./ml., the authors concluded that 1 gene determines resistance to 10 or more μgm./ml. Mutation apparently occurs independently but the mutation of the gene for high resistance is frequently associated with the simultaneous mutation of a gene determining a change to the large rough or elevated colonial morphology. *S. R. M. Bushby*

JANICKI, B. W. & PATNODE, R. A. **Enzymatic Determination of** *in vitro* **Lysis of Leukocytes by Tuberculin.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 311–14, 1 fig. [11 refs.]

"A method based on release of an intracellular lysozyme-like enzyme from lysed leukocytes was an acceptable substitute for microscopic cell counts in measuring tuberculin cytolysis of leukocytes from guinea pigs injected with heat-killed, human type, *M. tuberculosis*."

KONNO, K., NAGAYAMA, H. & OKA, S. **Nicotinamidase in** *Mycobacteria*: **a Method for distinguishing Bovine Type Tubercle Bacilli from other** *Mycobacteria* [Correspondence.] *Nature.* 1959, Nov. 28, v. 184 Suppl. No. 22, 1743–4.

A cell-free extract of ground tubercle bacilli, containing 2 mgm. of protein, produced 3·2–3·7 micromoles (μM) of ammonia from 10 μM of nicotinamide whereas a similar extract from bovine tubercle bacilli produced only 0·1 μM of ammonia. Extracts from avian tubercle bacilli, atypical acid-fast bacilli and non-pathogenic acid-fast bacilli contained either the same concentration or greater than the human variety for they produced 3·8, 3·2–3·3 and 6·8–7·4 μM of ammonia, respectively.

This procedure of measuring nicotinamidase was simplified by collecting the bacilli from cultures in Sauton media, washing them thrice with saline to remove ammonia from their surface, suspending them in saline to a concentration of 20 mgm./ml., placing 1 ml. of the suspension into each of 2 tubes, 1 containing 300 mgm. of nicotinamide in 1 ml. of 0·02 M phosphate buffer (*p*H 7·0) and the other containing 1 ml. of the phosphate buffer without nicotinamide. After incubating the tubes at 37°C. for 12 hours the presence of ammonia was detected with Russel's phenol-hypochlorite method; a positive test showed green blue and deep blue colour, and a negative test was amber.

By this simplified test 10 virulent, 3 attenuated and 2 isoniazid-resistant strains of human tubercle bacilli were positive, 6 of 7 virulent strains of bovine tubercle bacilli were negative, the 7th strain being weakly positive and 3 attenuated bovine strains were negative. 5 avian tubercle bacilli, 5 atypical acid-fast bacilli and 5 non-pathogenic acid-fast bacilli were all positive.

S. R. M. Bushby

PATTERSON, D. S. P. **Influence of Cobalt and Zinc Ions on the Growth and Porphyrin Production of** *Mycobacterium tuberculosis avium.* [Correspondence.] *Nature.* 1960, Jan. 2, v. 185, 57.

CLARK, Mary E. & FORREST, Elizabeth. **Growth Characteristics of Acid-Fast Microorganisms other than Tubercle Bacilli in HeLa Cells.** *Amer Rev. Respiratory Dis.* 1959, Nov., v. 80, No. 5, 744–6 9 figs. [10 refs.]

In this study approximately 100 strains of mycobacteria were examined by the tissue culture method described by SHEPHARD [this *Bulletin*, 1958, v. 33, 1176].

The photochromogens (Runyon's Group I) appeared to form a homogeneous group for they grew intracellularly in 2–3 days in filamentous form with parallel

sides and showed marked beading. The non-photochromogens of the Battey type (Runyon's Group III) also appeared to form a homogeneous group for they were irregular in shape and produced clubbed forms with definite branching but similar growth characteristics were seen with the avian tubercle bacillus and *Nocardia intracellularis*. 3 of the 12 strains of scotochromogens (Runyon's Group II) grew in a manner similar to those of the photochromogens, and the other 9 strains grew in a variety of forms. 6 of these scotochromogens and a number of non-chromogenic bacilli, considered to be contaminants, grew only extracellularly.

A few of the strains grew in an unusual form in that they were in small clumps, stained very irregularly, and seemed to form vacuoles; these strains came from patients with a mild but chronic pulmonary infection, which did not resemble tuberculosis, and the bacilli were resistant to isoniazid. *S. R. M. Bushby*

SCHLEGEL, H. G. Zur Carotinoidsynthese bei *Mycobacterium phlei*. [**Synthesis of Carotinoids in** *Mycobacterium phlei*.] *Zent. f. Bakt.* II. Abt. 1959, v. 113, Nos. 1/5, 71–9, 1 fig. [Numerous refs.]

POPE, C. G. & STEVENS, Muriel F. **The Properties of Crystalline Diphtheria Toxin-Protein: The Reaction of the Phosphate and Pepsin-Stable Antigens with Diphtheria Antitoxic Serum.** *Brit. J. Exper. Path.* 1959, Aug., v. 40, No. 4, 410–16, 3 figs.

Further observations on the complexity of crystalline toxin-protein obtained from culture of *C. diphtheriae* are presented [this *Bulletin*, 1957, v. 32, 1098; 1958, v. 33, 876, 877; 1959, v. 34, 483 *bis*].

The deoxyribonuclease described earlier as an element in diphtheria toxin has been found to appear in the crystalline product obtained from cultures in tryptic digest media but not in that from papain digest media.

A method for preparing a pepsin-stable fraction from crystalline toxin protein is described and it is shown that after treatment of toxin with $Na_2S_2O_3$ multiple diffusion lines are obtained in Ouchterlony plates in which such altered toxin diffuse against pepsin-refined antitoxin. 2 of these correspond to the pepsin-stable antigen and 1 to the phosphate-stable antigen described in an earlier paper.

The pepsin-stable and phosphate-stable antigens have been prepared in relative purity and give characteristic smooth flocculation curves with pepsin-refined antitoxin; the supernatants spun off from the precipitates, however, contain a high ratio of the specific antitoxin to diphtheria neurotoxin equally whether the non-specific antigen has been in excess of antitoxin or at low concentrations. Hence these antigens are distinct from the specific neurotoxin. *J. W. McLeod*

AGARWAL, S. C. & PRYCE, D. M. **Experimental Diphtheritic Paralysis in Rats.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 171–7, 8 figs. on 4 pls.

Toxin preparations of widely varying grades of purity were used but the effects were proportional to the estimated potency of the preparation in MLD. The lesions were best developed with a 20 MLD dose which the rats survived for up to 5 or 6 days. The most notable lesions were degenerative changes in the cortical and ganglion nerve cells. There was no evidence of interference with cholinesterase activity that could be demonstrated by the histochemical methods employed.

The distribution of lesions in nerve cells was very irregular. The cord was involved in some cases but never independently of brain lesions.

J. W. McLeod

CHANG, Kuang-Hou & LIANG, Yeh-Kai. [**Studies on the Nutrition and Respiration of** *Hemophilus influenzae*.] *Acta Microbiologica Sinica.* 1959, Dec., v. 7, No. 4, 341–5, 4 charts. [11 refs.] [In Chinese.] Eng'ish summary (9 lines).

LEIDY, Grace, HAHN, E. & ALEXANDER, Hattie E. **Interspecific Transformation in** *Hemophilus*; **a Possible Index of Relationship between** *H. influenzae* **and** *H. aegyptius*. *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 86–8.

"On the premise that the degree of reactivity of donor DNA with the heredity determinants of the recipient cell is a reflection of the degree of homology of the genome of donor and recipient cells, it has been proposed that transformation may serve as a valid criterion for bacterial taxonomy. If the use of single genetic marker, SM-resistance, provides a valid basis for comparison, *H. aegyptius* may be a member of the *H. influenzae* group."

See also p. 335, LJUTOV. **Technique of Indole Test.**

KAMPELMACHER, E. H. **On Antigenic O-Relationships between the Groups** *Salmonella, Arizona, Escherichia* **and** *Shigella*. *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 3, 289–324.

The relations between O antigens of members of the family Enterobacteriaceae were studied by testing boiled suspensions against several pools of antisera and then against individual members of pools which had agglutinated the test suspension. The antigens investigated were as follows: Salmonella, 1–52; Arizona, 1–33; *Escherichia coli*, 1–142 and OX 1 to OX 9; Shigella A1–10, B1–6, C1–15 and D. Absorption tests were made to prove the identity of cross-reacting antigens and antisera.

The findings confirmed and extended those of earlier workers and showed strong relationships between Arizona and Salmonella and between Escherichia and Shigella (shown by EWING *et al.* [this *Bulletin*, 1957, v. 32, 278] to have many antigens in common). Identical O antigens are shown in the table.

The results also show that it is not possible to prepare polyvalent sera that are group-specific for, as the author says, "There are no antigenic frontiers within the Family *Enterobacteriaceae*".

Indentical O-antigens of the *Salmonella*, *Arizona* and *Escherichia* groups.

Salmonella	*Arizona*	*Escherichia*
51	1, 2	
44	1, 3	
18	7ab	
50	9ac	55
41	13	
42	15	
38	16	
11	17	
35	20	111
21	22	
47ab	23	
16	25	
	28	118
52	31	
6, 14, 24	32	
	1, 33	123

S. T. Cowan

BACHRACH, U. **An Improved Method for the Determination of Lysine Decarboxylase Activity of Salmonellae.** *Amer. J. Clin. Path.* 1959, Dec., v. 32, No. 6, 580–81. [Reprinted from *Tech. Bull. Registry of Med. Technol.* 1959, Nov., v. 29, No. 11, 194–5.]

"A liquid medium consisting of Bacto peptone (0.5 per cent), Bacto yeast extract (0.3 per cent), glucose (0.1 per cent), *l*-lysine (0.5 per cent), lactose (1 per cent), and bromthymol blue (0.01 per cent) was used. The medium was adjusted to pH 6.2, distributed in 4–5-ml. amounts, and sterilized by autoclaving.

"The broth was inoculated with the test organism and incubated at 37°C. Results were read after 16 to 24 hr. All strains of Enterobacteriacae ferment glucose during the first 6 to 10 hr. of incubation and, thus, change the indicator to yellow. Lactose-negative bacteria, by decomposing lysine, subsequently change the color to blue. On the other hand, lactose fermenters retain their acidity regardless of their lysine decarboxylase activity, and the indicator remains yellow."

GHATAK, S. & SHRIVASTAVA, D. L., with the technical assistance of V. VARMA. **Studies in the Enzyme Make-up of** *Salmonella typhosa.* **Part IV. Organic Nitro-Reductase Activity.** *J. Sci. & Indust. Res.* New Delhi. 1959, Nov., v. 18C, No. 11, 213–16, 1 fig.

ŁUKJANIEC, A. & KEDZIERSKA, B. **The Use of Ion Exchange Resins for the Adsorption and Purification of Antigen** *Vi* **from** *Salmonella typhi. Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 8, 299–304.

By simple saline washing the Vi antigen can be extracted from a culture of *Salmonella typhi*, but it is in an impure state. Purification may be effected by adsorption onto, and elution from, fowl red blood cells and subsequent paper chromatography with water saturated with phenol as the mobile phase. In the present paper the authors describe their attempts to purify the native Vi antigen by trying to remove the unwanted proteins and polysaccharides by adsorption onto ion exchange resins pretreated with various electrolytes. Under the conditions of the experiments described there was no evidence of adsorption onto the resins used and any purification of the antigen was insignificant. When, however, the resin Dowex-2—a strongly basic anion exchanger, in the ionic form as Cl^- and OH^-—was pretreated with 1 M sodium formate and the antigen hydrolysed with acid for 1 hour, adsorption was complete but irreversible.

H. J. Bensted

ŁUKJANIEC, A. & KEDZIERSKA, B. **Tentative Identification of the Antigen** *Vi* **Functional Group combining Irreversibly with Ion Exchangers.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sc. Biol. 1959, v. 7, No. 9, 353–7.

The previous paper [see above] by these authors showed that hydrolysed Vi antigen, which remains haemagglutination-active, adsorbs irreversibly onto a Dowex-2 column pretreated with sodium formate, and cannot be liberated with hot acid. When Vi 1 phage was passed through a column the elution rate indicated that there was no specific adsorption of the phage onto a column covered with Vi antigen owing to the fact that the groups active for the phage were blocked on the ion exchanger. Receptors for the phage are not involved in adsorption onto the ion exchanger. When deprived of haemagglutinating activity by acid hydrolysis the antigen failed to adsorb onto the column, which suggests a relation between the combining power with the red cells and adsorption onto the ion exchanger.

H. J. Bensted

BRANDIS, H. & HOFMANN, S. Über Änderungen im Lysotyp bei Transduktion des Merkmals Beweglichkeit. [**Changes in Lysotype during Transduction of Motility**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 1/2, 65–70. [12 refs.]

5 non-motile strains of *Salmonella paratyphi B* were transduced with 3 different phages by the U-tube method with the object of recovering motile variants. From 1 strain of lysotype Jersey motile variants with i or b antigens were obtained which were resistant to all type phages or were of lysotype Beccles. A strain of lysotype 3a similarly yielded motile variants with b antigen of lysotypes Jersey and Beccles. The variants of altered lysotype were resistant to the transducing phage, and the change of lysotype was therefore ascribed to lysogenization.

D. J. Bauer

MITSUHASHI, S., KAWAKAMI, M., GOTO, S., YOSHIMURA, T. & HASHIMOTO, H. **Studies on the Experimental Typhoid. IV. The Microorganisms in the Organs of Infected Mice.** *Japanese J. Exper. Med.* 1959, Aug., v. 29, No. 4, 311–21, 9 figs. [20 refs.]

Mice injected intraperitoneally or intravenously with an attenuated strain of *Salmonella enteritidis* develop

in either case a bacteriaemia which persists for some hours, after which the organisms disappear from the blood stream but they are rapidly distributed through the body and may be detected in the liver, spleen and lymph nodes for several months after infection. This attenuated strain becomes established in organs such as the liver and spleen quite early on and begins to multiply attaining maximum growth in 24–48 hours. In contrast to the results obtained with a virulent strain, multiplication thereafter begins to decline. A chronic carrier state is set up and the mice show a steadfast resistance to superimposed infection by a virulent strain. In common with many other workers, the authors found that mice thus protected also carried the virulent challenge strain for long periods.

Mice infected with the attenuated strain when given a single dose of 0·3 mgm. dihydrostreptomycin within 18 hours of infection were found to be completely free of the infecting organism whereas after 24 hours intensive treatment with the drug produced no such effect. Mice developed the chronic carrier state in spite of the fact that the organism was fully sensitive *in vitro* to the drug.

A further point of interest is that evidence from centrifugal fractionation of suspensions of *in vivo* cultures in the early stages of the infection of the mice indicated that the organisms were significantly smaller than the cultures inoculated. On laboratory media, however, there was no suggestion of L-form populations; all the characters were identical with the parent culture.

[See also this *Bulletin*, 1959, v. 34, 926.]

H. J. Bensted

WATANABE, T. & WATANABE, M. **Transduction of Streptomycin Resistance in** *Salmonella typhimurium*. *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 16–29. [28 refs.]

WATANABE, T. & WATANABE, M. **Transduction of Streptomycin Sensitivity into Resistant Mutants of** *Salmonella typhimurium*. *J. General Microbiol.* 1959, Aug., v. 21, No. 1, 30–39, 2 figs.

VASSILIADIS, P. & MAQUET, R. Une nouvelle *Salmonella* isolée au Congo belge: S. Gombe (6,7: d: e,n,z15). [**A New** *Salmonella* **isolated in the Belgian Congo: S. Gombe**] *Ann. Inst. Pasteur.* 1959, Dec., v. 97, No. 6, 867–8.

The English summary appended to the paper is as follows:—

"The description is given of a new *Salmonella* serotype, isolated from the stools of a native 13 month old boy of the Belgian Congo: *S. gombe*: 6,7: *d* :*e,n,z*15."

ROHDE, R. & BISCHOFF, J. Ein neuer *Salmonella*-Serotyp: S. Eppendorf = 1,4,12,27:d:1,5. [**A New Salmonella Serotype: Salm. Eppendorf = 1,4,12,-27:d:1,5**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 1, 141–3.

JONES, R. L., HUTCHINSON, Joanne & CROFT, C. C. **A New** *Salmonella*-**Serotype: Salmonella Ohio.** *Pub. Health Lab.* 1959, Sept., v. 17, No. 5, 100.

"A new salmonella serotype, *Salmonella ohio* was isolated from the catheterized urine of a patient, following cholescystectomy. The antigenic formula was 6,7:b-1, w."

GOREA, A., with the technical collaboration of Ileana MĂLDĂRESCO. Recherches sur la kérato-conjonctivite des cobayes, déterminée par les germes du groupe *Shigella*. [**Investigations on the Kerato-conjunctivitis of the Guineapig caused by Germs of the** *Shigella* **Group**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, June, v. 18, No. 2, 245–55, 1 graph.

This is an affirmation of the value of the kerato-conjunctival reaction to instillation of *Shigella* cultures into the eyes of guineapigs as a specific diagnostic procedure for the identification of *Shigella* organisms. The intensity of the reaction is said to be directly related to the virulence of the particular culture. [See also SERENY, this *Bulletin*, 1958, v. 33, 690, 1959, v. 34, 567, 673.] *H. J. Bensted*

GRZYBEK-HRYNCEWICZ, Kryspina. Badania nad odpornością heterologiczną w obrebie podgrupy B pałeczek *Shigella*. [**Experiments on Heterologous Immunity within the** *Shigella flexneri* **Subgroup**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 3, 409–37. [36 refs.]

The English summary appended to the paper is as follows:—

"Experiments on homologous and heterologous immunity of dysenteric strains, subgroup B, were made using passive protective and agglutination tests. The cross reactions conditioned by the action of group antigens are, as a rule, lower than homologous ones which mainly depend on the action of type antigen. This concerns both the passive protection and agglutination. The passive, heterologous protection is however in some cases equal or higher than the homologous one. The same phenomenon can be observed when analysing the agglutination results. The heterologous immunity of X and Y variants which lack type antigens for other *S. flexneri* types, amounts to 19–61 per cent of the homologous immunity. These data suggest a high influence of group antigens on the production of immunity against dysentery on the immunisation with the bacilli from B subgroup. The heterologous immunity for the subtypes with a common type antigen comes to 23–100 per cent of the homologous immunity.

"It was shown that the dysentery bacilli from the subgroup B possess a varying range of heterologous immunity. A small range of immunity is a characteristic feature of types 4a, 4b and 6, a somewhat wider range of types 1a, 3, 5 and the widest of types 1b, 2a, 2b, X and Y.

"There is a partial correlation between the values

of passive protection and agglutination, no rules being established as to its incidence or absence."

GRZYBEK-HRYNCEWICZ, Kryspina & MULCZYK, Marian. Zmienność antygenowa pałeczek *S. flexneri* 1b. [**Antigenic Variability of *S. flexneri* Ib Strains**] *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1959, v. 7, No. 3, 439–60. [20 refs.]

The English summary appended to the paper is as follows:—

"Experiments on the antigenic variability of *S. flexneri* 1b strains were made on experimental animals and artificial media.

"*S. flexneri* 1b strains when passaged on white mice, were found to lose their type antigen I and to acquire type antigen III, the composition of group antigens remaining unaffected. Changes of this kind were exhibited by all 7 *S. flexneri* 1b strains used for passages. The changes in the antigenic structure seem to be permanent, as the strains maintained for 12 months on artificial media behaved in the agglutination as after immediate isolation from mice.

"No changes in biochemical properties could be found between parent and changed strains.

"Further experiments revealed that, besides type antigen III, the changed strains had acquired still an additional antigen, absent in other *S. flexneri* types. The physico-chemical properties of this antigen are most similar to ones of thermolabile α (15), β (10), γ and δ (16) antigens and identical with the properties of recently described thermolabile ϵ antigen (9). The additional type antigen of artificially obtained *S. flexneri* 3 variants is also serologically identical with antigen ϵ, which occurs in similar variants of this type, encountered in natural conditions (9)."

ISTRATI, G., GOREA, A., BARBER, Cella, ISTRATI, Maria & SORU, Eugenia. La vaccination antidysentérique. VI. Expériences de vaccination des souris avec 5 antigènes extraits d'une souche de *Sh. flexneri* type 2a, non-adsorbés ou adsorbés sur hydroxyde ou phosphate d'aluminium. [**Antidysenteric Vaccination. VI. Vaccination Experiments in Mice with 5 Antigens extracted from a Strain of *Sh. flexneri* Type 2a, adsorbed or not on Aluminium Hydroxide or Phosphate**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, June, v. 18, No. 2, 205–14.

In previous papers [this *Bulletin*, 1959, v. 34, 929] the same group of workers have described their immunization experiments with various extracts of *Shigella flexneri*. The work continues and in the present communication the antigens tested comprise extracts by trichloracetic acid, hot hydrochloric acid, ethylene, urea and distilled water at 80°C. either fluid or adsorbed on $Al(OH)_3$ or $AlPO_4$ and total in all 14 different preparations. Only 3 of these appeared to give promising results: the ethylene fluid extract, the same extract adsorbed on $Al(OH)_3$, and the hydrochloric acid extract adsorbed on $AlPO_4$. It is considered that these deserve further study.

H. J. Bensted

SERÉNY, B. **A New Method for the Investigation of *Sh. sonnei* Cultures.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 3, 179–89, 1 fig. [14 refs.]

By examining clearly isolated growing colonies of *Shigella sonnei* with a hand lens when the rays of light impinging on them are at different angles of incidence the author was able to obtain different pictures of colonial morphology. The colony with a central star-like picture was found to be characteristic of phase I *Sh. sonnei*. The moderately or slightly refractive colony with a homogeneous appearance nearly always indicated that the culture was in phase II, while a network patterned colony was indicative of a true R (rough) change. Serological tests with highly absorbed phase I, phase II and R sera fully confirmed these morphological observations. The central star of a smooth colony, in most instances, appeared to contain only phase I antigen while the periphery of the same colony contained phase II antigen. The colonies with the central star were virulent and the optically homogeneous, moderately refractive colonies were found to be avirulent.

H. J. Bensted

SERÉNY, B. *Sh. sonnei* **Cultures fermenting Salicin.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 3, 217–25. [17 refs.]

The author examined 69 strains of *Shigella sonnei*, already accepted as typical of their species, for their ability to ferment salicin and found 8 cultures brought about breakdown of this glucoside after an incubation period of 4–26 days; 5 strains were late saccharose-fermenters and 3 were non-saccharose-fermenters. Included in the series were also about 100 strains of recently isolated dysentery bacilli belonging to the Flexner group; none of these cultures fermented salicin. The fermentation reactions were checked by examining samples of salicin of different manufacturers and considerable care was taken to ensure that the culture media used for the tests undertaken contained no other fermentable substance. According to the accepted definition, organisms belonging to the *Shigella* group do not ferment salicin, and the author suggests that the definition should now be suitably modified.

H. J. Bensted

JANECEK, J., CHALOUPKA, J., VERES, K. & HAVRÁNEK, M. **Influence of DL-beta-Phenylserine on the Synthesis of Proteins in *Escherichia coli*.** [Correspondence.] *Nature.* 1959, Dec. 12, v. 184, Suppl. No. 24, 1895–6, 1 fig.

GIBSON, F. & WOODS D. D. **The Synthesis of Methionine by Suspensions of *Escherichia coli*.** *Biochem. J.* 1960, Jan., v. 74, No. 1, 160–72, 4 figs. [40 refs.]

HOLME, T., MALMBORG, A. S. & COTA-ROBLES, E. **Antigens of Spheroplast Membrane Preparations from *Escherichia coli* B.** [Correspondence.] *Nature.* 1960, Jan. 2, v. 185, 57–8.

NOMURA, M. & WATSON, J. D. **Ribonucleoprotein Particles within Chloromycetin-Inhibited** *Escherichia coli*. *J. Molecular Biol.* London. 1959, Sept., v. 1, No. 3, 204–17, 9 figs. [15 refs.]

TISSIÈRES, A., WATSON, J. D., SCHLESSINGER, D. & HOLLINGWORTH, B. R. **Ribonucleoprotein Particles from** *Escherichia coli*. *J. Molecular Biol.* London. 1959, Sept., v. 1, No. 3, 221–33, 3 figs. [33 refs.]

SPAHR, P. F. & TISSIÈRES, A. **Nucleotide Composition of Ribonucleoprotein Particles from** *Escherichia coli*. *J. Molecular Biol.* London. 1959, Sept., v. 1, No. 3, 237–9.

MEYNELL, G. G. **The Effect of Sudden Chilling on** *Escherichia coli*. *J. General Microbiol.* 1958, Oct., v. 19, No. 2, 380–89, 7 figs. [12 refs.]

"As found by earlier workers, *Escherichia coli*, growing in broth at 37° was rendered incapable of gross multiplication either on nutrient agar or in nutrient broth by sudden cooling in many diluents at 4°. Killing is due to the joint action of a suitable diluent and of sudden chilling, since survival was complete either after sudden chilling in 0.3M-sucrose or after gradual cooling in a potentially lethal diluent, such as Ringer's solution. Organisms in the stationary phase of growth were completely resistant. The susceptibility of growing organisms to sudden chilling changed rapidly during the exponential phase. Comparison with the survival after exposure to streptomycin, another bactericidal agent which has no effect on stationary phase cultures, showed that survival after chilling was not due to a fraction of the population being in the stationary phase.

"Sudden cooling of *Escherichia coli* strain B, infected with phage T2, had the same effect as ultrasonic disruption; namely, destruction of infective centres in the first half of the latent period followed, in the second half, by release of intracellular mature phage."

KATAGIRI, H. & TOCHIKURA, T. **Microbiological Studies of** *Coli-aerogenes* **Bacteria. Part VII. Degradation of Citrate.** *Bull. Agric. Chem. Soc. of Japan.* 1959, Nov., v. 23, No. 6, 475–81. [26 refs.] **Part VIII. The Occurrence of Isocitritase and Citritase.** *Ibid.*, 482–9. [35 refs.] **Part IX. On the Mechanism of Assimilation of Ammonia.** *Ibid.*, 489–92. [22 refs.]

UJVÁRY, G. Über die Serologie der *Klebsiella*-Gruppe und das Vorkommen der Serotypen in klinischem Material. [**The Serology of the Genus** *Klebsiella* **and the Type Distribution in Human Specimens**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 7/8, 481–95. [33 refs.]

The capsular antigens of 352 strains diagnosed as klebsiellas were determined in so far as the sera available (serotypes 1–30) allowed. 191 strains were typable, and type 16, with 75 strains, was much the most frequent in all the kinds of specimen (urine, sputum, pus, faeces) examined. Certain serotypes (within the 1–30 series) were not represented at all (9, 15, 19, 22, 23, 25, 26).

The biochemical reactions showed some variation from what is described as typical for *Klebsiella*.

	Typical	Found	
		+	−
Indole	−	42	310
MR	−	39 and 11 ±	302
VP	+	278	74
Citrate	+	339	13
Urease	+	325	27
Inositol	+	332	20
Motility	−	0	352

About half the strains were resistant to streptomycin, chloramphenicol, oxytetracycline and aureomycin, but only one strain was resistant to neomycin.

S. T. Cowan

CIUCĂ, M., STAMATESCO-EUSTATZIOU, Silvia, BARBER, Cella, VOINEA, Maria & TULPAN, Gertrude. Contribution à l'étude de la biologie des *Klebsiella*. I. Étude biologique et immunochimique de certaines souches de *Klebsiella*. [**Contributions to the Study of the Biology of Klebsiella. I. A Biological and Immunochemical Study of Some** *Klebsiella* **Strains**] *Arch. Roumaines Path. Expér. et Microbiol.* 1959, Sept., v. 18, No. 3, 347–59, 15 figs. [17 refs.]

EPSTEIN, S. S. **Experimental** *Klebsiella* **Pneumonia in Mice with particular reference to Periarterial Changes.** *J. Path. & Bact.* 1959, Oct., v. 78, No. 2, 389–96, 8 figs. on 3 pls. [23 refs.]

RAUSS, K. & VÖRÖS, S. **The Biochemical and Serological Properties of** *Proteus morganii*. *Acta Microbiologica.* Budapest. 1959, v. 6, No. 3, 233–48. [28 refs.]

222 strains of *Proteus morganii* were examined and in all the urease and phenylalanine tests were positive, all grew in KCN medium and produced indole; none produced gelatinase, or H_2S in a cystine-deficient medium but all were H_2S-positive when tested with a sensitive indicator (lead acetate papers) or cystine was added to the medium. All strains were MR-positive but the VP was variable. With tests which gave variable results (sucrose, galactose, raffinose, sorbitol, sorbose fermentations; VP, growth in citrate) it was possible to divide the strains into 12 biochemical groups which did not correlate with the serological groups. Serologically 29 "O" groups were found which, with 19 "H" antigens, enabled 57 serotypes to be defined.

In discussing the taxonomic position of Morgan's No. 1 bacillus the authors refer to "*P. Hauseri*, *P. Rettgeri*" as genera. They think that the Proteus group of the Enterobacteriaceae Subcommittee reports

should be regarded as a tribe, and each subdivision as a genus, of which Morgan's No. 1 would become *Morganella*, with only one species *Morganella morganii*.

S. T. Cowan

FITZ-JAMES, P. C. & YOUNG, I. Elizabeth. **Comparison of Species and Varieties of the Genus *Bacillus*. Structure and Nucleic Acid Content of Spores.** *J. Bacteriology*. 1959, Dec., v. 78, No. 6, 743–54, 12 figs. [27 refs.]

FITZ-JAMES, P. C. & YOUNG, I. Elizabeth. **Cytological Comparison of Spores of Different Strains of *Bacillus megaterium*.** *J. Bacteriology*. 1959, Dec., v. 78, No. 6, 755–64, 21 figs. [11 refs.]

FITZ-JAMES, P. C. **Morphology of Spores of *Bacillus apiarius* Katznelson.** *J. Bacteriology*. 1959, Dec., v. 78, No. 6, 765–8, 9 figs.

O'CONNOR, R. & HALVORSON, H. **Intermediate Metabolism of Aerobic Spores. IV. Alanine Deamination during the Germination of Spores of *Bacillus cereus*.** *J. Bacteriology*. 1959, Dec., v. 78, No. 6, 844–51, 6 figs. [26 refs.]

LINZENMEIER, G. Zur Methodik der Anaerobenzüchtung. Über die Eignung des Indikatorprinzips zur Wertbemessung anaerober Nährmedien. I. Mitteilung: Messung des Redoxpotentials unter anaeroben Verhältnissen. [**The Technique of Cultivating Anaerobes. The Value of the Indicator Principle for Assessing Anaerobic Culture Media. I. Estimation of Oxidation-Reduction Potential Levels under Anaerobic Conditions**] *Arch. f. Hyg. u. Bakt.* 1959, Nov., v. 143, No. 7, 537–60, 10 figs. II. Mitteilung: Die Reoxydation. [**II. Reoxidation**] *Ibid.*, Dec., No. 8, 561–86, figs. 11–15. [Numerous refs.]

The English summaries appended to the paper are as follows:—

I. "The time-course and the localization of oxidation-reduction processes occurring in sterile liquid nutrient media not inoculated with bacteria can be estimated by use of oxidation-reduction potential indicators. The method employing indicators is preferred to potentiometric and polarographic methods because it allows to follow up the oxidation-reduction processes with an accuracy sufficient for answering practical problems also when glass vessels commonly used for the cultivation of bacteria are employed. Oxidation-reduction potential levels occurring under anaerobic conditions, especially in the tubes devised by Gruber and characteristic for each peptone and each basal medium, e.g. liver infusion broth and meat infusion broth, can be determined. The determination of those potentials completes the test methods commonly applied to peptones and nutrient media, especially with respect to the suitability for the cultivation of anaerobic bacteria."

II. "It has been found that the degree and the velocity of the re-oxidation of nutrient media measured by oxidation-reduction potential indicators are suitable criteria for testing whether a nutrient medium is satisfactory for the cultivation of anaerobic bacteria. The following results have been obtained by sealing culture tubes in order to inhibit completely or to retard the re-oxidation: Vaseline is the most suitable compound, but oxygen in the air passes through paraffinum liquidum as well as through some of the silicon oils. The addition of small amounts of agar (0·05–0·1%) stabilizes the reduction capacity of liquid nutrient media and is also suitable for the simplification of the procedure described by Tarozzi. Due to the remarkable retardation of the re-oxidation by the addition of agar to liquid media, the lowest possible level of the oxidation-reduction potential occurring in liquid media can be determined by means of oxidation-reduction potential indicators in the lower not yet oxidized parts of a liquid medium filled into tubes."

MOSSEL, D. A. A., v. GOLSTEIN BROUWERS, G. W. M. & DE BRUIN, A. S. **A Simplified Method for the Isolation and Study of Obligate Anaerobes.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 290–91, 1 fig. on pl.

BONVENTRE, P. F. & KEMPE, L. L. **Toxicity Enhancement of *Clostridium botulinum* Type A and B Culture Filtrates by Proteolytic Enzymes.** *J. Bacteriology*. 1959, Dec., v. 78, No. 6, 892–3.

HICKS, R. Marian & CLARKE, Patricia H. **A Comparison of Glutamic and Aspartic Acid Decarboxylases of *Clostridium welchii*.** *Enzymologia*. The Hague. 1959, Nov. 30, v. 21, No. 3, 169–77. [18 refs.]

MEISEL-MIKOŁAJCZYK, F. **Antigen Composition of *Clostridium perfringens* Strains causing Food Poisonings.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 10, 387–93. [24 refs.]

2 strains of *Cl. perfringens* [*welchii*] were used, Nos. 480 and 543 from the Central Collection of strains of the Polish Academy of Sciences; they had been isolated from meat suspected to have caused food poisoning.

Acetone extracts were prepared for fractionation with organic solvents. Lipid components, 12% dry cell bulk, were stearic, palmitic, oleinic and one unknown acid; these were antigenically inactive by complement-fixation. All fractions contained sugars or glucosamine. In fractions with high protein content chromatography showed the presence of 12 amino acids: cystine, histidine, lysine, arginine, glycinoserine, aspartic and glutamic acids, proline, tyrosine, valine, phenylalanine and leucine; complement-fixation reactions were obtained at lowest dilutions. There were marked differences in the polysaccharide content of the various fractions from the 2 strains. All polysaccharides from both strains were serologically active.

With regard to specificity, fractions from strain 480 showed no cross reactions with antisera from *Cl. welchii* types B and F, but one fraction with a high polysaccharide content from strain 543 reacted with antisera from all *Cl. welchii* types.

It is emphasized that classification must depend on polysaccharide and not lipid or protein components.

Betty C. Hobbs

EASTOE, J. E. & LONG, Joan E. **The Effect of Nisin on the Growth of Cells and Spores of** *Clostridium welchii* **in Gelatine.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 1–7.

Cl. welchii type A, NCIB 6125, producing approximately 10^8 cells and 10^6 spores per ml. in Robertson's cooked meat medium after 18–20 hours at 37°C. was used; a few experiments were carried out with *Cl. bifermentans*, NCIB 506. The gelatin used contained approximately 5,000 aerobic bacteria per gm. and anaerobes not exceeding 1–2 per gm. The standard preparation of nisin contained 10^6 Reading Units (RU) per gm., of which 2 standard solutions were used containing 120 and 5,000 RU per ml. When counts of vegetative cells were required an initial dilution of 5×10^3 was made by transferring a standard loopful of the supernatant from an 18–20-hour cooked meat culture to 9 ml. of Ringer's solution. For spores a 1/10 dilution of the supernatant was immersed in water at 75°C. for 30 minutes to kill vegetative cells and activate the spores.

5% solutions of gelatin were sterilized and incubated with 1 ml. of the culture dilutions. Various amounts of nisin were added to the inoculated gelatin, and to the mixture was added ferric-sulphite-tryptone medium; after incubation of the tubes for 18 hours at 37°C. dense black colonies were counted.

The development of vegetative cells was prevented by the presence of 2 Reading Units (RU) of nisin per ml. of final culture medium, although the effective concentration may have been 6 RU per ml.; approximately 40 RU per ml. prevented colony formation from spores. When gelatin containing nisin was stored a considerable proportion of the activity of the antibiotic was still present after 5 weeks. The effect of a given level of nisin may depend on nutrients and particularly *p*H; reducing the *p*H of the medium diminished the growth of both spores and cells of *Cl. welchii*. It was suggested that the food manufacturer should add nisin during the preparation of the gelatin solution. In a 2% solution a final level of 40 RU per ml. would be required corresponding to 2,000 RU per gm. or 10^6 RU per pound of dry gelatin. The authors suggest that this would be uneconomic for general use, but where damage to an expensive product is possible it might be contemplated; special instances rather than widespread use would be preferable. *Betty C. Hobbs*

GOUDIE, J. G. **The Nature of a Neutralising Substance for** *Clostridium welchii* **Alpha-Toxin in Faeces.** *J. Path. & Bact.* 1959, July, v. 78, No. 1, 17–28.

In view of failure to find α toxin of *Clostridium welchii* in the faecal contents and the known and constant presence of that clostridium in the human gut, the α toxin neutralizing property of filtrates from faecal fluids was investigated.

The methods of estimating this toxin worked out by OAKLEY and WARRACK [this *Bulletin*, 1942, v. 17, 503] have been used and parallel investigations with (1) a standard antitoxin preparation, (2) a preparation of serum lipoids, (3) a dialysed solution of trypsin and (4) dialysed faecal filtrates, have been made. It has been shown that the variations in amount of toxin neutralized with dilution, with varying time of contact of the reagents before addition of the indicator (sheep's red cell suspension) and with variation in temperature during contact of toxin and inhibiting agent all bring the faecal filtrate into line with the proteolytic enzyme rather than with the antitoxin or lecithin preparations.

Besides this, the effect of the faecal filtrates can be shown to be removed by the trypsin inhibitor, soya bean meal extract, provided dilutions are carefully adjusted to avoid the α toxin neutralizing effect of that reagent.

It is concluded, therefore, that the gut is normally protected from *Cl. welchii* toxin by its natural digestive enzymes.

[See also this *Bulletin*, 1957, v. 32, 904.]

J. W. McLeod

BACTERIOPHAGES

BRENNER, S., STREISINGER, G., HORNE, R. W., CHAMPE, S. P., BARNETT, L., BENZER, S. & REES, M. W. **Structural Components of Bacteriophage.** *J. Molecular Biol.* London. 1959, Sept., v. 1, No. 3, 281–92, 11 pls. & 5 figs. [43 refs.]

VELAUDAPILLAI, T. **Serological Grouping and Thermal Death Points of** *S. virchow* **Bacteriophages.** *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 146, No. 2, 176–84. [14 refs.]

On the results of cross-neutralization tests with phage antisera, 158 phages obtained from lysogenic strains of *Salmonella virchow* were divided into 8 serological groups. These, like phages from *Salm. typhi-murium* [BOYD, this *Bulletin*, 1951, v. 26, 1111] were further subdivided into (i) 2 Group A phages, killed by heating at temperatures between 75° and 90°C. and (ii) 6 Group B phages, killed at temperatures between 56° and 80°C.

Janice Taverne

UETAKE, H. & UCHIDA, T. **Mutants of** *Salmonella* **Phage e^{15} with Abnormal Conversion Properties.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 495–505, 1 fig. [16 refs.]

MURAKAMI, W. T., VAN VUNAKIS, Helen & LEVINE, L. **Synthesis of T2 Internal Protein in Infected *Escherichia coli*, Strain B.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 624–35, 6 figs. [30 refs.]

"The synthesis of the internal protein of T2 bacteriophage has been studied. Net synthesis was observed 2–3 minutes after infection and prior to the formation of viral DNA. Chloramphenicol caused complete cessation of the synthesis of internal protein and also affected DNA synthesis. Treatment of the phage with ultraviolet light resulted in normal synthesis of internal protein in the absence of net increase in DNA. Proflavine did not affect either synthesis of DNA or of internal protein, but prevented phage maturation."

KOCH, G. & HERSHEY, A. D. **Synthesis of Phage-Precursor Protein in Bacteria infected with T2.** *J. Molecular Biol.* London. 1959, Sept., v. 1, No. 3, 260–76, 8 figs. [26 refs.]

KAUFMAN, Eleanor & HIATT, C. W. **Photodynamic Action of Proflavine on T2 Coliphage.** [Correspondence.] *Virology.* New York. 1959, Nov., v. 9, No. 3, 478–9, 1 fig.

Proflavine added to cultures of bacteria infected with T2 or T4 phage is known to suppress the production of infective phage [this *Bulletin*, 1946, v. 21, 475; 1956, v. 31, 73]. It is reported here that proflavine also acts on mature T2 phage, outside the bacterial cell, rendering it sensitive to inactivation by visible light. Survival curves are given for phage preparations exposed to light after varying periods of incubation with proflavine in the dark. No unusual morphological changes were observed under the electron microscope, and it is not suggested that abnormal structures seen in proflavine lysates are derived from mature particles inactivated in this way. *Janice Taverne*

LOVELESS, A. & STOCK, Jocelyn C. **The Influence of Radiomimetic Substances on Deoxyribonucleic Acid Synthesis and Function studied in *Escherichia coli* Phage Systems. IV. Colony-Forming Ability and Phage-Synthetic Capacity of *Escherichia coli* Strain *B* and Two of its Mutants following Alkylation.** *Proc. Roy. Soc.* Ser. B. 1959, Nov. 3, v. 151, No. 942, 129–47, 12 figs. [23 refs.] **V. A Comparison of the Inactivation of Phages *T2*, *T7* and Two Strains of *T4* by Alkylating Agents.** *Ibid.*, 148–55, 7 figs. [12 refs.]

IV. Cells of *Escherichia coli* B which had lost the ability to form colonies as a result of treatment with the nitrogen mustard di(2-chloroethyl)methylamine (HN 2) were, it was found, still able to support the multiplication of phages T2 and T7. *E. coli* B was more sensitive to inactivation by HN 2 than were 2 strains derived from bacteria which had been grown in the presence of HN 2, but all 3 strains were more sensitive to fresh than to stale (and therefore cyclized) reagent. Survival curves of all 3 strains treated with the monofunctional alkylating agent ethylenimine were of the "multihit" type, whereas curves for the bifunctional HN 2 were downwardly concave. The synthesizing capacity of all 3 strains of *E. coli* B for both phages T2 and T7 was reduced to the same degree by treatment with either the mono- or the bi-functional agent.

V. Phages T2 and T7 were treated with the alkylating agents di(2-chloroethyl)methylamine (HN 2) and ethylenimine, and survival curves determined. The 2 phages were equally sensitive to freshly prepared HN 2, but T7 was more sensitive than T2 to stale HN 2 and to ethylenimine, which are both ionized in solution. It is concluded therefore that cations can penetrate more easily into T7 than T2. 2 strains of T4, 1 sensitive and 1 resistant to osmotic shock, were also found to show differences in sensitivity towards the reagents, the strain sensitive to osmotic shock behaving like T2 and the resistant strain like T7.

[See also this *Bulletin*, 1959, v. 34, 1186.]
Janice Taverne

HOLLOWAY, B. W. & MONK, Marilyn. **Transduction in *Pseudomonas aeruginosa.*** [Correspondence.] *Nature.* 1959, Oct. 31, v. 184, Suppl. No. 18, 1426–7. [10 refs.]

It is reported that phage P 110 active on strain 1 of *Pseudomonas pyocyanea* can transduce various markers governing the nutritional requirements of the bacteria from a prototrophic donor strain to different auxotrophic mutants of the same strain. The transfer of genetic material was inhibited by phage antiserum but not by crystalline DNase, providing additional evidence that the phage itself was responsible for the transfer.

These experiments, which parallel transduction by phage P22 in *Salmonella* [this *Bulletin*, 1953, v. 28, 745], and by phages P1 and 363 in *Escherichia coli* [*ibid.*, 1956, v. 31, 566, *bis*], are taken as further evidence for believing that the phenomenon of transduction is a general one. *Janice Taverne*

STINEBRING, W. R. & BRAUN, W. **Brucellaphage.** *J. Bacteriology.* 1959, Nov., v. 78, No. 5, 736–7, 1 fig.

The authors have confirmed that a strain of *Brucella* phage obtained from Russian workers produced plaques on smooth and intermediate strains of *Br. abortus* (not on rough strains), but did not lyse *Br. suis* or *Br. melitensis* strains. They observed that secondary, resistant, colonies of *Br. abortus* growing in areas of confluent lysis were mucoid and rough, thus supporting the claim of PARNAS [this *Bulletin*, 1958, v. 33, 1180] that *Brucella* phages may "induce" dissociation.
Janice Taverne

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Enteric group; Arthropod-borne group; Others.**

MARCUS, P. I. **Host-Cell Interaction of Animal Viruses. II. Cell-Killing Particle Enumeration: Survival Curves at Low Multiplicities.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 546–63, 4 figs. [Numerous refs.]

LITWIN, J. **The Growth Cycle of the Psittacosis Group of Micro-Organisms.** *J. Infect. Dis.* 1959, Sept.–Oct., v. 105, No. 2, 129–60, 42 figs. [44 refs.]

This study was made with the virus of feline pneumonitis growing on the chorio-allantois of 10-day chick embryos. No evidence was obtained that the virus multiplied in a non-infectious state or that it arose by condensation from an undifferentiated sheet of viroplasm. Multiplication appeared to be by binary fission. The virus particles produced early in the growth cycle differed from the elementary body—an end product of the cycle—in being larger and flatter, less virulent and more labile on storage. The author is not convinced that the elementary body is the sole end product of the growth cycle, as maintained by BEDSON and his colleagues [this *Bulletin*, 1934, v. 9, 852; 1935, v. 10, 479; 1954, v. 29, 1004; 1959, v. 34, 1297]. He finds evidence of the production of late large forms as well. *S. P. Bedson*

MATUMOTO, M., OMORI, T., HARADA, K., INABA, Y., MORIMOTO, T. & ISHII, S. **Miyagawanella: Psittacosis-Lymphogranuloma Group of Viruses. 10. Effects of Antibiotics and Sulfonamides in developing Hen's Eggs on Goat Pneumonitis Virus, Bovine PL Virus and Psittacosis Virus isolated in Japan.** *Japanese J. Exper. Med.* 1959, Oct., v. 29, No. 5, 445–55. [69 refs.]

"In view of the susceptibility of Miyagawanella viruses to various antibiotics and chemotherapeutic agents, goat pneumonitis, bovine PL, and psittacosis viruses which were isolated in Japan were studied in developing eggs in this respect. All the viruses tested were found to be susceptible to tetracycline, chlortetracycline, oxytetracycline, erythrocin, penicillin and chloramphenicol, but not significantly susceptible to streptomycin and sulfonamides (sulfisomidine, sulfadiazine, glucosulfone sodium, and acetosulfamine). The antibiotics of the tetracycline group and erythrocin were very active and penicillin and chloramphenicol were less so."

HAHON, N. **Survival of Variola Virus in Chorio-allantoic Membrane Preparations.** *J. Bacteriology.* 1959, Nov., v. 78, No. 5, 731–3.

Frozen suspensions of variola virus maintained their titres for 2–3 years at − 60°C. and − 25°C. At 4°C. and 25°C. infectivity had vanished by the 64th and 16th weeks respectively Dried preparations of the same virus suspensions maintained their titres for 3 years at − 60°C., − 25°C. and 4°C. At 25°C., however, there was a steady decline in infectivity from $10^{9\cdot5}$ IU [infectious units]/gm. at the start to $10^{2\cdot5}$ IU/gm. after 3 years. As the author points out, this is still enough virus to be the cause of disease if variola virus naturally dried is as stable. *Colin Kaplan*

VIEUCHANGE, J. Réaction de fixation d'hématies en cultures de cellules infectées de variole. [**The Haemadsorption Reaction in Cells in Culture Infected with Variola Virus**] *Bull. Soc. Path. Exot.* 1959, July–Aug., v. 52, No. 4, 432–7, 5 figs. on 2 pls. [12 refs.]

The results in this paper confirm the findings of other workers [DRIESSEN and GREENHAM, this *Bulletin*, 1959, v. 34, 1187] that vaccinia-sensitive fowl erythrocytes adhere specifically to cells in culture infected with vaccinia or variola viruses. This was shown with 3 cell lines: HeLa, RH (human kidney) and RB1 (bovine kidney). The adherence of erythrocytes occurred in infected cell cultures before there were any microscopically recognizable changes in the cells. Later, when cytopathic change was obvious, the positions of areas of infection (*i.e.* plaques) were emphasized by the attachment of erythrocytes to the damaged cells.
Colin Kaplan

PUMPER, R. W., ALFRED, L. J. & SACKETT, D. L. **Multiplication of Vaccinia Virus in Serum-Free and Serum-Containing Cell Cultures.** [Correspondence.] *Nature.* 1960, Jan. 9, v. 185, 123–4.

Using derivatives of a mouse lung cell line growing in medium with or without the addition of serum, the authors found that the IHD-E strain of vaccinia virus attained the same titre whether serum was present in the medium or not. They think this information may be useful in smallpox vaccine production at some future date. *Colin Kaplan*

FURNESS, G. & YOUNGNER, J. S. **One-Step Growth Curves for Vaccinia Virus in Cultures of Monkey Kidney Cells.** *Virology.* New York. 1959, Nov., v. 9, No. 3, 386–95, 2 figs. [11 refs.]

One-step growth experiments were done with vaccinia virus in both suspensions and monolayers of monkey kidney cells. Some monolayer cultures infected at low multiplicity were washed and incubated as monolayers; others were suspended in medium and incubated as diluted suspensions of cells. Assays for infected centres were made by plating cells on monolayer cultures. The efficiency of plating was high. The experiments showed an eclipse period of 8–10 hours and a yield of 300 plaque-forming units per infected cell in suspensions 24 hours after infection. Adding antivaccinial rabbit serum

to a suspension of cells reduced the numbers of infected centres by about 20-fold.

After sonic disruption of infected cultures treated with serum there was about 50-fold less infectious virus than in washed cultures or cultures treated with deoxyribonuclease (DNAase). When the disrupted cells were treated with antiserum or DNAase or both after serum treatment of monolayers there was very much less (50–100-fold) infectious virus than in monolayers treated with DNAase both before and after sonic disruption. The authors incline to the view that this indicates 2 types of recoverable infectious particle about half of which are susceptible to antibody. *Colin Kaplan*

JOKLIK, W. K.; RODRICK, J. McN. **Biochemical Studies on Vaccinia Virus in Cultured Cells. I. Incorporation of Adenine-8-C^{14} into Normal and Infected Cells** [JOKLIK & RODRICK]. *Virology*. New York. 1959, Nov., v. 9, No. 3, 396–416, 4 figs. [27 refs.] **II. Localization of Adenine-8-C^{14} incorporated in the Course of Infection** [JOKLIK, W. K.]. *Ibid*., 417–24, 1 fig.

I. With HeLa cell cultures labelled with adenine-8-^{14}C, the authors followed changes in the nucleic acid content and radio-activity of various cell fractions during the 36 hours after infection of the cultures by sufficient vaccinia virus to give almost 100% infection. Only the RNA of the microsomal fraction showed any change: there was a small increase of not more than 40%. No changes were demonstrable in the DNA of either the nuclear or mitochondrial fractions. Vaccinia virus (which contains DNA) is found in the mitochondrial fraction. More labelled adenine was incorporated into the microsomal RNA of infected cells than into uninfected cells. The greater rate of incorporation was at about 10 hours after infection—at about the time of first appearance of new infectious virus. Similar patterns of labelled adenine incorporation were found in Eagle's KB cells and Earle's L strain cells infected with vaccinia virus.

II. In the second paper it is shown that the increased amount of labelled adenine in the microsomal fraction of cells infected with vaccinia virus is certainly incorporated into cytoplasmic RNA and not into DNA or into a small but highly active RNA species.

Colin Kaplan

OVERMAN, J. R. & SHARP, D. G. **Ratios of Vaccinia Virus Particles to Virus Infectious Units. Studies of Ratio Changes during Growth and Adaptation in Eggs, Guinea Pigs, and Rabbits.** *J. Exper. Med.* 1959, Sept. 1, v. 110, No. 3, 461–80, 5 text figs. & 10 figs. on 2 pls. [18 refs.]

The authors determined the ratios between vaccinia virus particles and infectivity in preparations of several sorts. During multiplication of virus in chick embryo chorio-allantois the particle/infectivity ratio increased from the 1st day of infection to the 6th. In the later stages the morphology of the virus particles seemed to be different. During passage of calf lymph vaccinia virus in chorio-allantoic membrane the particle/infectivity ratio remained substantially the same in 9 passages, suggesting that the virus needs no adaptation to be able to multiply in this host. On the other hand, the ratios found during serial passage of chick embryo virus in rabbit indicated that some form of adaptive change was taking place. The changes in ratio consequent on adaptation to a new host were well shown during serial passage in guineapig skin. Of 5 attempts to adapt vaccinia virus to the guineapig only 1 was successful. In this series the ratio increased to 200 in the 2nd passage but by the 8th had decreased to 16. In another series, the ratio of 21 in the 1st passage increased to 500 in the 2nd and the virus was lost. In 3 other attempts the virus was lost after the 2nd passage.

The authors suggest "that the ratio of particles to infective units found during adaptive passage will be an index of the general susceptibility of that animal to the virus used . . . lowest ratios will indicate lowest resistance . . ." *Colin Kaplan*

MAYYASI, S. A., SCHUURMANS, D. M. & BROWN, A. **The Agglutination of L Cells by Vaccinia Virus. I. The Agglutination and Agglutination-Inhibition Titrations for Virus and Antibody.** *J. Immunology*. 1959, Oct., v. 83, No. 4, 411–17, 5 figs. [15 refs.]

When the IHD strain of vaccinia virus was added to cultures of Earle's L strain mouse cells, the cells were agglutinated. This reaction reached its greatest intensity at about 24 hours. The Minnesota strain of vaccinia virus, however, was often a poor agglutinator, even in high concentration. Appropriate controls showed the agglutination reaction to be specific. The cell-virus mixtures had, however, to be incubated at 37°C. It was also clearly shown that the L-cell agglutination was not produced by the soluble haemagglutinin associated with vaccinia virus, but depended on the presence of infectious vaccinia virus. A linear relationship was demonstrated between agglutination titre and mouse LD50. The lower limit of sensitivity of the method appeared to be about 10^5 mouse LD50 per ml.

Inhibition of agglutination was used to titrate anti-vaccinial and anti-variolous sera. Comparison of these titrations with titrations by pock neutralization and by mouse intracerebral neutralization showed inhibition of L-cell agglutination to be much more sensitive and precise than the mouse test and measurably more sensitive than the pock neutralization test. *Colin Kaplan*

TAVERNE, Janice & WILDY, P. **Purification of Herpes Simplex Virus by Chromatography of Calcium Phosphate.** [Correspondence.] *Nature*. 1959, Nov. 21, v. 184, Suppl. No. 21, 1655–6, 2 figs. [10 refs.]

Attempts to purify herpes simplex virus were carried out by chromatography on calcium phosphate columns [TAVERNE *et al*., this *Bulletin*, 1959, v. 34, 498]. Infective materials obtained from embryonated eggs or from HeLa cell cultures were added to columns and eluted with increasing concentrations of phosphate buffer at *p*H 7·0. When infected chick embryo allantoic fluid was used, infective virus was recovered

mainly in 2 fractions corresponding to 0·4 and 0·7–0·8 M phosphate eluates. At least 50% of the original infectivity was recovered. Complement-fixing antigen was recovered mainly in the 0·2 M eluate. It was shown by protein estimations that a considerable degree of virus purification was achieved.

The elution patterns of virus materials obtained from infected HeLa cells varied according to the nature of the starting material. Extracellular virus present in culture fluids and virus liberated from infected cells by versene treatment were eluted in a single peak at 0·4 M phosphate concentration. In contrast, intracellular virus obtained by disrupting versene-treated cells was eluted in 2 bands with peaks at 0·4 and 0·7 M phosphate. This finding suggests that cell-associated virus may differ from free virus in physico-chemical properties. *H. G. Pereira*

LEPPELT, H. & SÖLTZ-SZÖTS, J. Serologische Studien zum Herpes-simplex-Problem. [**Serological Studies on the Herpes Simplex Problem**] *Arch. f.d. gesamte Virusforschung*. 1959, v. 9, No. 1, 127–34, 1 fig. [37 refs.]

An investigation has been made of the course of development of complement-fixing antigens to herpes V and S antigens in guineapigs infected intraperitoneally, intranasally, or by dermal scarification. Antibodies appeared after 1–2 weeks and reached maximum titres after 5 weeks, the V titres being considerably higher than the S titres; no difference in titre was observed between the animals immunized by different routes. Antigens prepared from infected chorioallantoic membranes gave higher titres than antigens prepared from tissue cultures. After 9 weeks all the animals were susceptible to reinfection by dermal scarification. *D. J. Bauer*

FRASER, K. B. **Features of the MEL × NWS Recombination Systems in Influenza A Virus. I. The Effect of Age of the Mouse on the Intracerebral Growth of the MEL Strain of Influenza A Virus.** *Virology*. New York. 1959, Oct., v. 9, No. 2, 168–77, 2 figs. [13 refs.] **II. The Formation of N-M, Recombinant, Strains of Influenza A Virus in Mouse Brain.** *Ibid.*, 178–90. [18 refs.] **III. The Pathogenicity of Recombinant Neuro-MEL Viruses grown in Mouse Brain and Chick Embryo Brain.** *Ibid.*, 191–201, 1 fig. [12 refs.] **IV. Increments of Virulence during Successive Cycles of Double Infection with Two Strains of Influenza A Virus.** *Ibid.*, 202–14, 1 fig. [23 refs.]

I. Mice of different ages were inoculated intracerebrally with a non-neurotropic (MEL) strain of influenza A virus. Egg-infectivity titrations of brain suspensions from mice killed after intervals ranging from 2½ hours to 5 days after inoculation revealed limited multiplication of infective virus, the titres reached being inversely proportional to the age of inoculated mice. Treatment of brain suspensions with crude cholera filtrate resulted in increased infectivity titres throughout the period of observation suggesting that some of the residual as well as newly formed infectious virus is bound to inhibitors. This behaviour of MEL virus was not affected by concomitant infection by a neurotropic (NWS) virus except where recombinant forms (described in the following papers) were recovered.

II. Double infection of newborn or adult mice with MEL and NWS virus strains inoculated intracerebrally in equivalent doses gave rise to recombinant N-M forms. These recombinants could not be detected in brain suspensions from mice killed less than 12 hours after inoculation but were regularly isolated after this time, when the infectivity titres of brain suspensions exceeded that of the residual inoculum. This indicates that recombinants are formed in the mouse brain and not in the eggs used for infectivity titrations. Most of the infective virus formed in brains in which recombination takes place is neutralized by both MEL and NWS antisera whereas double neutralization was never observed with viruses from brain suspensions free of recombinants. Evidence is presented suggesting that doubly-neutralizable virus particles give rise to both parent and recombinant strains. Possible analogies of virus recombination with bacterial transformation are discussed.

III. N-M recombinants isolated from mice or chick embryos doubly inoculated with NWS and MEL strains by the intracerebral route were tested for mouse and chick embryo pathogenicity. 29 recombinants isolated from mouse brains and 50 recombinants from chick embryo brains showed a comparable distribution of mouse and chick embryo virulence, strains of low virulence predominating in both groups. It is suggested that mouse brain and chick embryo pathogenicities of NWS and N-M strains are genetically linked or dependent on variations of a given heritable quality. Recombinant strains varied in virulence for mice inoculated by the intracerebral or intranasal routes and no correlation was observed between these 2 types of mouse-pathogenicity.

IV. N-M recombinants obtained from double infection of chick embryo brains with NWS and MEL were propagated, together with the parent NWS strain, through 4 serial passages in chick embryo allantoic cavity. Virus multiplication was limited to a single cycle during each passage. 3 N-M recombinants used to initiate each series of passages were pathogenic for chick embryos but not for adult mice, when inoculated intracerebrally. Clones isolated at limit dilutions at each passage level were tested for mouse virulence and showed a gradual increase in neuropathogenicity, resembling in some ways the stepwise increase of bacterial drug resistance brought about by transforming agents.

It is suggested that these results may be due either to the acquisition by the N-M strain of virulent genes from NWS or to the transfer of virulence suppressor or modifying genes from N-M to NWS at each cycle of double infection. Neither of these hypotheses could account, however, for occasional appearance of virus progenies which were less virulent than the parent strains. As an alternative explanation consistent with the last findings, it is proposed that the virus action on

host cells is in some ways analogous to that of bacterial transforming principles. *H. G. Pereira*

FRASER, K. B., NAIRN, R. C., MCENTEGART, M. G. & CHADWICK, C. S. **Neurotropic and Non-Neurotropic Influenza-A Infection of Mouse Brain studied with Fluorescent Antibody.** *J. Path. & Bact.* 1959, Oct., v. 78, No. 2, 423–33, 8 figs. on 2 pls. [19 refs.]

The localization of influenza A viruses inoculated intracerebrally into newborn and adult mice was studied by means of the fluorescent antibody technique. A non-neurotropic strain (MEL) was compared with the neurotropic strains NWS and N-MEL, the latter being a recombinant derived from MEL and NWS. Antisera were labelled by conjugation with lissamine rhodamine B200.

The distribution and intensity of fluorescence in brains of newborn mice examined 15 to 17 hours after inoculation with NWS or MEL was comparable and involved mainly the membranes (leptomeninges, ependyma choroidal epithelium) with, in addition, discrete parenchymal foci proportional in number to the size of virus inoculum. Similar results were obtained with adult mice, except that parenchymal fluorescence was totally absent or limited to very few cells. In brains of mice killed 5 to 7 days after inoculation, NWS virus was widespread through the parenchyma in young mice and regularly present in Ammon's horn, the Purkinje cell layer of the cerebellum and the brain stem in adult mice. In contrast to this, the late stages of infection by MEL virus was associated with focal parenchymal fluorescence in young mice whereas practically no staining was observed in adult animals. The behaviour of the neurotropic recombinant N-MEL was similar to that of the neurotropic parent (NWS) strain. *H. G. Pereira*

ZAKSTEL'SKAIA, L. I. & EFIMOVA, V. A. **Histopathological Changes in the Lungs of Mice infected with Mouse-Adapted and Unadapted Variants of A-Prime Influenza Virus.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 305–11, 2 figs. [Translated from Russian.]

JAMES, Suzanne M. & FISET, P. **Serum Inhibitors of Asian Strains of Influenza Virus.** [Correspondence.] *Nature.* 1959, Nov. 21, v. 184, Suppl. No. 21, 1656–7.

The high sensitivity of certain strains of Asian influenza virus to normal horse serum inhibitors was lost abruptly in the course of serial egg passages. The change from sensitive to insensitive state was favoured by adding normal serum to the virus inoculum used for serial passages. Loss of sensitivity to normal serum haemagglutination inhibitor was associated with resistance to the virus neutralizing activity of normal horse serum. The inhibitor-resistant virus eluted more rapidly and more completely from red cells than did the sensitive strains. *H. G. Pereira*

MCKINNEY, R. W., ENGLAND, Beatrice L. & FROEDE, Suzanne. **Studies with Hemadsorption Virus Type 1. I. Recovery from Two Cases of Influenza-Like Disease in Military Personnel and Related Investigations.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 280–96, 4 figs. [14 refs.]

Haemadsorption type 1 (Para-influenza 3) virus [this *Bulletin*, 1958, v. 33, 621, 711] was isolated from throat washings of 2 young adults with febrile acute upper respiratory disease. Properties of the strain isolated from one of these patients were investigated in detail. It was propagated, causing cytopathic effect in cultures of monkey kidney, HeLa cells and human amnion (FL) cells. The cytopathic effect caused in HeLa cells was characterized mainly by syncytial formation. It could also be propagated in the amniotic cavity of fertile eggs. It did not cause apparent disease in newborn mice inoculated by the intracerebral and peritoneal routes, in 21-day-old mice inoculated intranasally, in rabbits inoculated intravenously or in hamsters inoculated intranasally. The hamsters showed, however, marked antibody rises. The virus agglutinated human group O, guineapig and, less regularly, chicken erythrocytes. Haemagglutination was best observed at room temperature. Virus elution from red cells was rapid at 37°C.

No serological relationship could be detected between the virus under study and Coxsackie group A, types 1 to 10, Coxsackie group B types 1 to 5, poliovirus types 1 to 3, Q fever, ECHO viruses types 1 to 13, adenovirus types 1 to 8, herpes simplex, Newcastle disease virus, mumps, influenza A, B and C, croup-associated virus, lymphocytic choriomeningitis, western equine, eastern equine and St. Louis encephalitis viruses. It did show some antigenic relationship with Sendai virus especially when convalescent human sera were used. Both patients from whom the virus under study were isolated showed, apart from homologous antibody responses, rises in neutralizing, complement-fixing and haemagglutination inhibiting antibodies for Sendai virus. A serological survey gave results suggesting that haemadsorption type 1 or some antigenically related virus is responsible for widespread human infection. *H. G. Pereira*

GRANOFF, A. **Studies on Mixed Infection with Newcastle Disease Virus. I. Isolation of Newcastle Disease Virus Mutants and Tests for Genetic Recombination between them.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 636–48, 4 figs. [12 refs.] **II. The Occurrence of Newcastle Disease Virus Heterozygotes and Study of Phenotypic Mixing involving Serotype and Thermal Stability.** *Ibid.*, 649–70, 1 fig. [17 refs.]

FÖLDES, P., SZERI, I. & BÁNOS, S. **Virological Investigations during the 1957 Epidemic of Poliomyelitis in Hungary.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 3, 257–62.

During 1957 there was an extensive outbreak of poliomyelitis in Hungary mainly due to type 1 poliovirus.

During this epidemic faeces from 55 paralytic patients were examined in fibroblast tissue cultures and a virus was isolated from 21 of them. 13 of these proved to be type 1 poliovirus and 1 type 2 poliovirus. None of the 7 strains not neutralized by poliovirus antiserum were pathogenic for suckling mice. 3 of them were strains of ECHO 11 and 1 ECHO 7. The remaining 3 strains belonged to 2 distinct serological types of unidentified virus. These unidentified viruses were not neutralized by antisera to the first 19 ECHO virus types (excluding types 10, 16 and 18). The high incidence of enteroviruses other than poliovirus from cases of paralytic poliomyelitis raised the question of the aetiological relationship of these strains to the disease. Unfortunately, paired sera were only available from 2 of the patients and both of these showed antibodies both to type 1 poliovirus and to the strain isolated. 214 sera obtained from children undergoing orthopaedic treatment for the late results of poliomyelitis were examined and 95% had type 1 antibodies and all contained antibodies to at least one type of poliovirus. The question of the aetiological role of the ECHO viruses isolated from cases of paralytic poliomyelitis remains uncertain.

A. J. Beale

LE BOUVIER, G. L. **The D→C Change in Poliovirus Particles.** *Brit. J. Exper. Path.* 1959, Dec., v. 40, No. 6, 605–20, 7 figs. [28 refs.]

Le Bouvier has recently described a quantitative technique for measuring and distinguishing the C and D antigens of poliovirus [this *Bulletin*, 1960, v. 35, 316]. This technique has now been used to analyse the change from D to C. Infectious poliovirus preparations contain D antigen and, in varying degrees, C antigen. On heating D is destroyed and C concurrently increases [*ibid.*, 1959, v. 34, 834] and the evidence is that D is converted into C rather than that D is destroyed and C concurrently "unmasked". Heat inactivation of D antigen appeared to be a first order reaction with an activation energy of 203 kcals. per mole. The author is careful to point out that observations were made over a narrow range of concentration (4-fold) and of temperature (48°C.–52°C.). The exact rate of heat inactivation of D antigen is probably affected by many factors as is illustrated by the effect of horse serum. This was found to increase the rate of D-C conversion, and similarly "washed" virus was inactivated more slowly than crude concentrates. Heat destroys D antigen and infectivity at similar rates but ultraviolet light (UVL) destroys infectivity much faster (about 30-fold) enabling non-infectious D antigen to be obtained. As with heating so UVL treatment appears to cause D-C conversion. In 1 of 2 UVL inactivation experiments, destruction of D proceeded exponentially, in the other there was evidence of a "multi hit" type of curve.

The *p*H of the agar used for the precipitin tests was found to be important. Thus at *p*H below 3 no D or C lines were obtained. D antigen, except for type 2, was unaffected down to *p*H 4–5. C lines, except for type 1, failed to appear at *p*H 6 or below. On the alkaline side D antigen lines disappeared first at *p*H 8 for type 3 and 9–10 for types 1 and 2. Above *p*H 12 no lines were seen. These effects appeared to be exerted on the antigens.

Other agents were found to affect the D-C change. Thus some, for example lyophilization (no technical details are given: for all other experimental procedures these are fully given) caused D-C change just as drying did at high temperatures. Other agents accelerated the effect of temperature. In high concentration they enabled the temperature effect to be noted at 37°C. or lower, and in lower concentrations they enhanced the rate of D-C change at 50°C. Other agents acted as inhibitors. An accelerating effect of temperatures is as follows. Virus concentrate stored at 4°C. for 3 months left the D content unchanged but caused an increased rate of destruction at 50°C. compared with an aliquot of the same concentrate stored at − 23°C. Incorporation of mercuric chloride 0·002% or merthiolate 0·01% (even 0·001% for type 3) in the agar destroyed the D antigen precipitin line, but the presence of 0·07% versene and 0·01% merthiolate prevented the destruction of the D antigen of types 1 and 2 though some effect on type 3 was still noticeable. Versene was also effective in counteracting mercuric chloride. Merthiolate (0·1%) at 4°C. had only a very slight effect in reducing the amount of type 2 and 3 D precipitate. Pretreatment of virus concentrates with phenol for 1 hour at 37°C. appeared to convert D to C and at higher concentrations destroy C. Thus treatment of virus with water-saturated phenol as in GIERER and SCHRAMM's (*Ztschr. f. Naturforsch.*, 1956, 11b, 138) technique for the release of infectious viral RNA destroyed all the C and D antigen. Similarly, 1% phenol which was without effect on the D antigen content nonetheless accelerated the conversion rate at 50°C.

All the treatments if prolonged or made stronger destroyed both C and D. Similarly, both type differences and almost certainly strain differences exist. Thus C antigen is destroyed in 1 minute at about 75°C. for type 3, about 80°C. for type 2 and about 85°C. for type 1. The majority of the tests were done with 50-fold concentrates of virus effected by ultracentrifugation of Brunhilde for type 1, YSK for type 2 and Leon for type 3. Strain differences are suggested by the fact that the MEF 1 strain of type 2 differed from YSK in response to *p*H, thus both D as well as C of MEF 1 were destroyed at *p*H 6·0. It was found that the D-C change was retarded in hypertonic sodium chloride. Thus at 0·5 M the inactivation rate at 52°C. was 1/10 of that at 0·14 M. At higher molarities the inactivation was so slow as to be impracticable to measure. Suggestive evidence was also obtained that formaldehyde (0·1% for 5 weeks at 4°C.) and L cystine (0·01% for 30 hours at 37°C.) retarded the inactivation of type 1 at 50°C.

[This and the paper preceding it [Le Bouvier, *ibid.*, 1960, v. 35, 316] are of first rate importance. Confusion between D and C antigen has bedevilled attempts to establish simple serological methods for the diagnosis of poliomyelitis or the measurement of the immunizing antigen content of poliovaccine.] *A. J. Beale*

EGGERS, H. J. & SABIN, A. B. **Factors determining Pathogenicity of Variants of ECHO 9 Virus for Newborn Mice.** *J. Exper. Med.* 1959, Dec. 1, v. 110, No. 6, 951–67, 1 fig. [21 refs.]

The original prototype strain of ECHO 9 virus (Hill) [this *Bulletin*, 1955, v. 30, 554] was not pathogenic for suckling mice. Since that time a great variety of ECHO 9 viruses have been isolated from patients with abacterial meningitis and a febrile exanthem in Europe and North America which are pathogenic for suckling mice. It has been a common observation that first passage tissue culture fluids are more pathogenic for suckling mice than the original specimen from the patient. In this paper the factors determining the pathogenicity of ECHO 9 virus for newborn mice have been analysed. It was found necessary for a mouse pathogenic strain to be able to multiply rapidly in mice inoculated under 24 hours of age so that by the time they were about 4 days there were 10^8 TCD50 present in the mouse. Strains unable to achieve this titre were non-pathogenic. This was because about 5–6 days of age there was a marked change in the susceptibility of mice to large doses of virus. Some strain of ECHO 9 virus of which the prototype Hill strain is an example were totally unable to multiply in mouse tissues and were not adsorbed to them. Other strains were capable of varying rates of multiplication. Strains with a very poor rate of multiplication might be incapable of ever reaching the necessary critical titre by day 4. Other strains could do so provided they were administered in sufficiently high dosage whereas occasional strains could multiply in mice so rapidly that very small doses caused typical Coxsackie A type lesions in mice. Most ECHO 9 virus strains in man were only capable of very slow rates of multiplication in suckling mice and therefore large doses were required to produce paralysis and this is the explanation for the rarity of isolation of the virus directly from patients. Propagation of the virus in tissue culture did not select strains that could grow quickly in mice but successive passages in mice did this. The authors' experiences with ECHO 9 virus from healthy children does not support the idea of ARCHETTI *et al.* [this *Bulletin*, 1959, v. 34, 1194] that virulence for mice is associated with strains isolated from patients. They support the grouping of ECHO, Coxsackie and polioviruses together into one family known as enteroviruses. *A. J. Beale*

FRANKLIN, A. E. & SINCLAIR, J. C. **Tissue Culture Studies with Infectious Hepatitis Specimens.** *Canadian J. Microbiol.* Ottawa. 1959, Dec., v. 5, No. 6, 567–71. [12 refs.]

"Twenty-nine human adult and eight monkey tissues were studied in culture. The addition of prednisolone to growth media restricted the growth to epithelial-like cells and also provided a slight growth stimulus. Thirty-four specimens of acute hepatitis origin failed to provide indications of virus. Detroit-6 cells were cultured in synthetic media supplemented with sheep serum. Sixteen experiments were inoculated with 82 specimens of acute hepatitis origin. There were no conclusive results with this line of cells."

ADA, G. L. & ANDERSON, S. G. **The Infectivity of Preparations made by the Action of Phenol on Dengue I, Dengue II, GD VII and Herpes Simplex Viruses.** [Correspondence.] *Australian J. Sci.* 1959, May, v. 21, No. 8, 259–60.

From the brains of infant mice infected with certain neurotropic viruses a material considered to be ribonucleic acid has been extracted by treatment with phenol. In an experiment with dengue I virus the titre of the initial brain material was 10^6 and of the ribonucleic acid extracted from it $10^{0.6}$, and with dengue II the corresponding titres were 10^5 and $10^{0.8}$. Treatment with ribonuclease abolished the infectivity of the presumed ribonucleic acid but did not affect the virus. Similar results were obtained with GDVII virus, but no infective ribonucleic acid could be extracted from herpes virus. *D. J. Bauer*

ANDERSON, S. G. & ADA, G. L. **Murray Valley Encephalitis Virus: Preparation of an Infective "Ribonucleic Acid" Fraction.** *Australian J. Exper. Biol. & Med. Sci.* 1959, Aug., v. 37, Pt. 4, 353–64. [12 refs.]

Infective "RNA" was prepared from baby mouse brains infected with Murray Valley encephalitis virus by extraction of a brain suspension with 90% phenol followed by ether extraction of the resulting supernatant. Infectivity was titrated by inoculation on to the chorio-allantoic membrane of embryonated eggs, the endpoint being taken as embryo death by 72 hours. The infectivity of the starting material was always higher than that of the RNA extracted, and when various methods of titration in chick embryos and mice were compared, the differences in titre were lowest on the chorio-allantoic membrane. Higher titres were obtained when the membrane was dropped with the inoculum than when the membrane was dropped before inoculation. When the RNA was heated in the presence of a suspension of normal mouse brain, its heat-stability was about the same as that of the intact virus. Some RNA preparations were markedly less stable than the average and this appears to be due to residual tissue ribonuclease in the preparations. 3 phenol treatments gave more stable preparations than 1. Normal rabbit serum was found to inhibit or destroy the infectivity of RNA at dilutions up to 1 in 10,000. The inhibitor was heat stable at 37°C. and 56°C. but sensitive to 62°C. Tissue extracts from spleens and lungs of mice contained inhibitor titring 1:4,000 to 1:35,000. The amount of inhibitor in serum was not reduced by splenectomy. Neither inhibitor nor ribonuclease affected the intact virus. Extracts of normal mouse brain and liver were found to protect RNA from destruction by inhibitor or ribonuclease. The protective agent in these extracts was heat labile, but was not

sedimented by 93,000 *g* for 90 minutes. A neutralization test on virus derived from the RNA confirmed that it was Murray Valley virus.

It is evident from this paper that for the preparation of stable infective RNA, ribonucleases in the associated tissue must be eliminated. *C. E. Gordon Smith*

MOLNÁR, E. **Some Biological Properties of a Hungarian Strain of the Tickborne Encephalitis Virus. Adaptation of Virus to the Embryonated Egg and Chick Embryonic Tissue Cultures.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 1, 23–33, 6 figs. [34 refs.]

The KEm_1 strain of tick-borne encephalitis virus isolated from ticks in Hungary [this *Bulletin*, 1954, v. 29, 1203] and having undergone 70 mouse passages, was used. Chick embryos inoculated by the allantoic, amniotic and yolk sac routes showed slowing of movements after 3–6 days and soon died. Affected embryos had widespread petechiae on the epidermis and in those with longer incubation periods there was gross oedema of subcutaneous tissue from which virus could be isolated. These changes were prevented when the virus was neutralized with immune serum. After about 9 passages by the allantoic or yolk sac routes, its virulence by yolk sac inoculation increased, but its virulence for mice was little affected. By daily passage with heavy inocula in Maitland-type chick embryo tissue cultures the virulence for eggs was maintained, but the mouse virulence declined so that there was a 2 log difference after 10 passages, 4 log after 29, and 6 log after 45 tissue culture passages. The low mouse-virulence strain was identified with the original virus by neutralization tests *C. E. Gordon Smith*

CHAMBERLAIN, R. W., SUDIA, W. D. & GILLETT, J. D. **St. Louis Encephalitis Virus in Mosquitoes.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 221–36, 3 figs. [24 refs.]

Experiments were undertaken to assess the vector potential of *Culex quinquefasciatus* [*fatigans*] and *C. pipiens* for St. Louis encephalitis virus, because they appear to be the vectors in areas where *C. tarsalis* is too scarce. The BFS-968 strain of St. Louis virus isolated from *C. tarsalis* after 2 mouse passages was used. Mosquitoes were infected by feeding on viraemic chicks and transmission studies made by feeding the mosquitoes on ½-day-old chicks after various incubation periods. The chicks were later tested for viraemia.

High transmission rates (mostly 90–100%) were obtained with 5 strains of *C. quinquefasciatus* and 3 of *C. pipiens*. There was no evidence of transovarial infection. The extrinsic incubation period of 1 strain of each species was studied in detail and it was found that after 4–6 days more virus was present in the *C. pipiens*; after 13–17 days the virus levels in the 2 species were again about equal. This corresponded with more rapid development of the ability to transmit in *C. pipiens*: 100% after 12 days' incubation compared with 18–29% in *C. quinquefasciatus*, which did not reach 100% transmission until after about 26 days. By feeding mosquitoes on older chicks with low levels of viraemia, the dose of virus necessary to infect 5% of mosquitoes (the threshold) was determined to be $10^{0.2}$–$10^{1.4}$ mouse LD50 for 5 strains of *C. quinquefasciatus* and about $10^{1.2}$ LD50 for a strain of *C. pipiens*. A half to a third of the mosquitoes infected in these experiments were able to transmit. The avidities of strains of *C. pipiens* and of *C. quinquefasciatus* for biting man and chickens under laboratory conditions were compared. Only 1 strain (of *quinquefasciatus*) showed a greater avidity for chickens under the experimental conditions. Recently colonized *C. quinquefasciatus* had generally low feeding rates. Several other mosquito species were fed on viraemic chicks: only small numbers of *Culex restuans* and *Culex salinarius* fed, but almost all of these became infected and were able to transmit. 58–84% of *Aëdes dorsalis* fed became infected, but only 4–16% transmitted. About a third of the *Aëdes triseriatus* and *Psorophora confinnis* fed became infected, but 20% and 7% were the maximum transmission rates. Only 3 of 34 *Aëdes aegypti* became infected, but 2 of them transmitted. Infection was established in 1 or 2 each of *Anopheles quadrimaculatus*, *Mansonia perturbans* and *Wyeomyia vanduzeei*. None of 4 *Aëdes vexans* fed became infected. *C. E. Gordon Smith*

SUDIA, W. D. **The Multiplication of St. Louis Encephalitis Virus in Two Species of Mosquitoes: *Culex quinquefasciatus* Say and *Culex pipiens* Linnaeus.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 237–45, 3 figs. [15 refs.]

A strain of *Culex quinquefasciatus* [*fatigans*] after more than 100 laboratory generations was compared with a strain of *C. pipiens* after about 30 generations in the laboratory. The BFS-968 strain of St. Louis encephalitis was used. Mosquitoes were inoculated intrathoracically with virus by microcapillary pipette. The ratio of mouse LD50 to mosquito LD50 for these species was found to be between 10:1 and 25:1.

After inoculation of 0·7 mouse LD50 of virus, mosquitoes were ground up at intervals and inoculated into mice. In *C. quinquefasciatus* virus was first detected after 60 hours, after which the titre rose steadily to $10^{4.7}$ LD50 after 96 hours and $10^{5.9}$ LD50 at 144 hours. In *C. pipiens* virus became detectable at 48 hours and the maximum of 10^6 LD50 was reached by 96 hours. When 700 LD50 were inoculated, no significant difference was demonstrated between the mosquito species—maximum titres were found after 72 hours.

Large numbers of both species were inoculated with about 0·1 LD50. These were fed on ½-day-old chicks at intervals and the chickens tested for viraemia 60 hours later. From the third day onwards 100% infection rates were found in both species. 33% of *C. quinquefasciatus* transmitted after 5 days, 90% after 6 days and 100% after 8 days. 12% of *C. pipiens* transmitted after 3 days, 43% after 4 days, 61% after 5 days and 100% thereafter. With inoculation of 330 LD50 95% of both species transmitted at 3 days and 100% thereafter.

Thus, after small doses of virus multiplication of virus and transmission occurs earlier in *C. pipiens* than in *C. quinquefasciatus*. *C. E. Gordon Smith*

LAVILLAUREIX, J., GRUNER, J. E. & VENDRELY, R. L'encéphalite à virus West Nile au microscope électronique. Etude virologique et histopathologique. **[Virological and Histopathological Studies of West Nile Virus by Means of the Electronic Microscope]** *C.R. Soc. Biol.* 1959, v. 153, No. 7, 1241–4, 2 figs.

A suspension of mouse brain infected with West Nile virus was purified by precipitation at an acid *p*H followed by chloroform-alcohol extraction. In chromium-shadowed preparations the virus was seen to be spherical and about 35 mμ in diameter. Ultra-thin sections of infected KB cell cultures showed virus particles in large and small groups in the nuclei sometimes close to the nuclear membrane. In cells where the nucleus had lost its structure numerous virus particles could be seen in the cytoplasm adherent to the nuclear membrane. In sections of embryonic mouse-brain cultures similar groups of virus particles were seen. In sections of infected mouse brain the nuclear changes were similar; in the cytoplasm the virus particles were associated with the Nissl granules. Virus multiplication was observed in glial and endothelial cells as well as in neurones.

C. E. Gordon Smith

PORTERFIELD, J. S. **A Plaque Technique for the Titration of Yellow Fever Virus and Antisera.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, Nov., v. 53, No. 6, 458–66, 3 figs. (2 on 2 pls.).

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 363.]

COLLIER, W. A., DE ROEVER-BONNET, H. & HOEKSTRA, J. **Some Experiments with Dilution Media for Yellow Fever Virus in Virus Titrations.** *Trop. & Geograph. Med.* Amsterdam. 1959, Sept., v. 11, No. 3, 197–205, 24 graphs. [12 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 362.]

MEERS, P. D. **Adaptation of the 17D Yellow Fever Virus to Mouse Brain by Serial Passage.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1959, Nov., v. 53, No. 6, 445–57, 5 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 361.]

COLLIER, W. A. & DE WIT, M. J. **Culture of Yellow Fever Virus 17D in Ascites of Krebs-2-Carcinoma.** *Trop. & Geograph. Med.* Amsterdam. 1959, Sept., v. 11, No. 3, 281–6, 6 graphs. [16 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 360.]

MATUMATO, M., MUTAI, M., OGIWARA, H., NISHI, I., KUSANO, N. & AOYAMA, Y. Isolement du virus de la rougeole en culture du tissu rénal du Singe. **[Isolation of Measles Virus in Monkey Kidney Tissue Culture]** *C.R. Soc. Biol.* 1959, v. 153, No. 5, 879–83.

The following is a translation of the authors' summary:—

From pharyngeal secretions of 15 patients with measles seen in Tokyo in 1957–58, 4 strains of the virus were isolated in monkey kidney tissue culture. Identification was made by comparison of the cytopathogenicity and serological specificity with those of the Edmonston strain.

IMMUNITY

GRABAR, Pierre & MIESCHER, Peter. [Edited by.] **Immunopathology. 1st International Symposium. Basle/Seelisberg 1958.** pp. xv + 520, numerous figs. 1959. Stuttgart. Basle: Benno Schwabe & Co., Steinentorstrasse 13 (Petrihof), Switzerland. [Sw.fr. 65.–.]

The first International Symposium on Immunopathology, held at Seelisberg, Basel, in June 1958, was arranged to promote discussion between immunologists and clinicians upon topics in which an association between immunization and pathological changes is known or suspected.

51 scientists from Europe and U.S.A. participated and 43 papers were presented; these are published in full in the original language (25 English, 8 French and 10 German) and each paper is summarized in the other two languages. The discussion which followed each paper or group of papers is published in abbreviated form in one language, usually English or German.

The text is arranged in the following six sections:—

(1) *General immunopathology* (3 papers). These introductory papers consist of a historical review of immunopathological concepts and discussions on the pathogenic mechanism of immune reactions and the problems involved in reconciling the auto-antigenicity of tissue constituents with immunological theory.

(2) *The properdin system* (1 paper). An informative review of the properties and clinical significance of properdin.

(3) *Agammaglobulinaemia* (2 papers). An extensive review of the group of conditions and observations on two series totalling 46 cases.

(4) *Organ-specific immunopathology*. Observations in human disease and in experimental animals upon organ-specific antibodies relating to the kidney (3

papers), liver (1 paper), spermatozoa (2 papers), thyroid gland (3 papers) and a paper on humoral antibodies to homografts.

(5) *Inflammatory immunoreactions.* 2 papers on the influence of thyroid functional status upon inflammatory reactions and the detoxifying properties of tissue iron, 6 papers on the immediate allergic and Arthus reactions, 2 papers on delayed allergic reactions, 3 papers on the pathogenic properties of antigen-antibody complexes, and 2 papers on the Shwartzman phenomenon.

(6) *Rheumatoid arthritis and disseminated lupus erythematosus.* The rheumatoid agglutinating factor (4 papers), immunoreactions in rheumatoid arthritis (2 papers), the serology of disseminated lupus erythematosus (4 papers) and the relationship between rheumatoid arthritis and disseminated lupus erythematosus (3 papers).

The moderate delay in appearance of this volume may detract slightly from its value to the research worker with a particular interest in one or more of the subjects. The greatest value of the book resides, however, not in any one particular section, but in the width of the topics covered, and the delay in publication is more than justifiable by the very high standards of editorship, printing and binding. In all sections, there are well documented reviews, the methods described for detecting antigen-antibody reactions are both numerous and ingenious, and the uninhibited discussions following many of the papers provide some assessment of the reliability of the techniques employed and the validity of interpretation.

The largest, and perhaps the most important section, is that on inflammatory immunoreactions. This serves to emphasize the need for continued fundamental research in order to solve one of the major problems in immunopathology, namely, the difficulty in establishing that a particular antibody is responsible for the pathological changes accompanying its development.

In conclusion, it should be emphasized that this is a volume of lasting value, well indexed in three languages, and with extensive lists of important recent references.

J. R. Anderson

ANN. INST. PASTEUR. 1959, Nov., v. 97, No. 5, 613–752, numerous figs. [Numerous refs.] Colloque Annuel de la SOCIÉTÉ FRANÇAISE DE MICROBIOLOGIE. 1re Journée: 11 Juin 1959. Problèmes généraux d'Immunologie [**General Problems of Immunity**].

GRABAR, Pierre. *Protein antiprotein reactions* (pp. 613–625). In making the introduction to an annual colloquium of the French Society of Microbiology on the general problems of immunology, Grabar discusses the features in protein structure which are responsible for stimulating antibody formation. He takes into account Landsteiner's classical experimental work on this subject and its application in view of our advancing knowledge of protein structure. Mention is made of Singer's work which suggests that carboxyl groups are more important in this connexion than amino, sulphur combined or phosphorylated groups. The contrasts between "polyosides" and deoxyribonucleic acids acting as haptens or antigens and proteins with long and complicated peptide chains is emphasized and attention is drawn in particular to the existence of multiple antigenic sites located on such chains distinct from one another and not necessarily related to the terminal groups of the chain. The difficulty of conceiving the sites of antigen antibody combination on protein chains of helicoidal structure is discussed.

Finally, the value of combined observation on electrophoresis and immune reactions by formation of lines of precipitation of antigen by antibody is emphasized and among many applications of this method the possibility of determining 24 separate constituents in human serum is mentioned.

LAPRESLE, Claude. *Heterogeneity of antibodies to proteins* (pp. 626–635). In the following communication detail is given of some of the work on which the conception of multiple and distinct antigenic sites on the protein molecule outlined in Grabar's introduction is founded. This consists of a study of the precipitation reactions between antibody to human serum obtained from the rabbit and a comparison with similar reactions with antibodies to human serum digested or partly digested with a variety of enzymes, trypsin, pepsin, chymo-trypsin and extract of rabbit spleen.

Immuno-electrophoresis applied to these various antigens reacting against rabbit serum prepared with the intact serum albumin demonstrates that the original antigen can be resolved to at least 3 components each reacting with a different antibody already present in the antiserum produced with the intact protein. They conclude, therefore, that multiple and different antigenic "sites" exist in the whole molecule, that antisera will contain appropriate antibodies and that these may be produced in different amounts by different animals. This conception obviously implies a greatly increased complexity in the nature of antigen antibody reactions and their interpretation.

RAYNAUD, M. and RELYVELD, E. H. *The diphtheria toxin-antitoxin reaction* (pp. 636–678). The authors discuss this reaction at great length to show how the simpler earlier theories on this subject must give place to far more complex ones. They have already reviewed much of this work in numerous papers.

The main points made are that the toxin antigen should be assumed to be a protein of multiple antigenic sites to which separate antibodies are formed, several of these are capable of producing precipitates with the corresponding antibody but not of neutralizing the toxin since the toxic "site" gives rise to a separate antibody. The latter gives rise to neutralizing but not to precipitating antibodies hence the correspondence of flocculating titre and neutralizing titre in any serum depends on how the 2 or more varieties of antibody are blended. The standard international serum is one which gives a good correspondence of flocculating and neutralizing antibody but many others do not, especially those derived from horses which were Schick-positive at the outset of immunization. This hypothesis appears, they claim, to explain better than others the Danysz phenomenon and POPE's observation [this *Bulletin*, 1953, v. 28, 485] that, by special absorption of fractions, a neutralizing serum devoid of flocculating activity can be obtained.

The sources of error in flocculation observations, dependent on variations of the concentration of the

total product antibody antigen in a series of tubes are discussed and a method for overcoming them recommended. The varying valency of toxins in their capicity to combine with a greater or lesser number of molecules of antibody is also discussed and described as ranging from 4 to 12·5.

One phrase in the authors' summary of their findings may well be applied to much similar work—"*L'hypothèse nous paraît plus utile, formulée en ses termes les plus vagues qu'agrémentée de fausses précisions.*"

It is further emphasized that in the immunization of Schick-negative horses carried to the stage of hyper-immunization, the antiserum is at first mainly gamma globulin passing over later to beta globulin and that although the last are normally produced on account of their higher experimental titre, the first are probably more valuable because of the greater avidity of the antibody and a greater tissue penetrating power due to a composition more nearly akin to the human serum globulin.

DUBERT, J.-M. *The hapten-antihapten reaction* (pp. 679–696). This chapter will only be followed in its detail by those who have a considerable knowledge of the more recent developments in biochemistry and physical chemistry as well as familiarity with the phenomena of immunity.

Amongst the conclusions drawn are that even a hapten of well defined composition will, when combined with a protein to form an antigen, give rise to multiple antibodies of differing although related affinities. Further, it is maintained that precipitating antibodies are divalent and that the closer investigation of hapten-antihapten reactions only serves to emphasize the remarkable specificity of the phenomenon of antibody formation which, in this respect, is unique, going beyond the specificity of induced enzymes.

RELYVELD, E. H. & BEN EFRAIM, S. *The diphtheria toxin* (pp. 697–717). TURPIN, A. and RAYNAUD, M. *The tetanus toxin* (pp. 718–732). These two papers are largely reviews of the literature bearing on their subjects and give considerable detail of the authors' findings in the purification of these toxins.

The paper on tetanus toxin includes a discussion of the size of the molecule in crystalline toxin and its modification by chemical processing designed to effect de-polymerization.

VAN HEYNINGEN, W. E. *The receptor of tetanus toxin in the nervous system* (pp. 733–751). This last paper is an account in French of the work already communicated by Van Heyningen to the *Journal of General Microbiology* and reviewed by this *Bulletin* [1959, v. 34, 944 *ter*].

J. W. McLeod

NAJJAR, V. A. [Edited by.] **Immunity and Virus Infection. Symposium held at Vanderbilt University School of Medicine, May 1–2, 1958.** pp. viii + 262, numerous illustrations. [Numerous refs.] 1959. New York 16: John Wiley & Sons, Inc., 440 Fourth Avenue, N.Y. London: Chapman & Hall, Ltd., 37, Essex Street, W.C.2. [84s.]

This book contains a collection of 20 papers presented at a symposium held at the Vanderbilt University School of Medicine in 1958. The individual contributions range over a very wide field, and some bear only a tenuous relationship to the subject defined in the title; their general tenor is theoretical, and little new experimental work is described. The first paper is by SIR MACFARLANE BURNET, on *The Theories of Antibody Production* (pp. 1–17). Three main theories have been put forward so far to explain the production of antibodies. The Haurowitz-Pauling theory postulates that the antigen acts as a direct template which impresses specificity upon globulin molecules. The indirect template theory of Burnet and Fenner postulates that the antigen brings about a mutation in certain cells as a result of which they acquire the inheritable ability to produce antibody. The latest theory to be developed is the clonal selection theory of Burnet, in which it is assumed that cells already exist which can produce a globulin which will react with the antigen, and that complementary relationship between antibody and antigen becomes closer as the result of mutation and selection of a clone of cells which can produce globulin giving a better fit. The performances of the 3 theories in explaining various fundamental propositions in immunity are admirably compared in a table, from which it is evident that the only theory which can explain everything (or nearly everything) is that of clonal selection. The subject is continued by F. HAUROWITZ, in a paper on *The Rôle of the Antigen in Antibody Formation* (pp. 18–25). If the antigen acts as a direct template it should persist in the body as long as antibody is being produced, and it should therefore be possible to find it by using techniques with sufficient sensitivity. Antibodies labelled with radioactive atoms persist in the organs for many months, and by means of autoradiography can be demonstrated in the cytoplasm of the Kupffer cells and in the red pulp of the spleen. The degree of radioactivity observed is consistent with the presence of several hundred molecules of antigen in each cell. An objection to the direct template theory is the difficulty of explaining the anamnestic reaction, but Haurowitz postulates that this is due to the release of preformed antibody, and by the use of a very ingenious experimental technique it has been possible to obtain evidence supporting this view. A. M. PAPPENHEIMER JR., in *The Delayed Hypersensitive State and Its Possible Relationship to Antibody Formation* (pp. 26–30), considers that there cannot be any satisfactory alternative to the direct template theory in view of the unlimited number of antibody configurations which can be produced by a cell.

The symposium next passed on to a consideration of immunological tolerance, which was reviewed by R. D. OWEN (*Immunology of Tissue Transplantation and Tolerance*, pp. 31–37), H. KOPROWSKI (*An Approach to the Biology of Tumors and Viruses through Consideration of Tolerance and Congenital Defects*, pp. 38–49) and R. E. BILLINGHAM (*Some New Aspects of Immunological Tolerance with Respect to Homologous Living Cells*, pp. 50–55). Recent work has provided evidence which suggests that immunological tolerance persists after the cells which have induced it have disappeared from the body, since newborn mice injected with spleen cells from an F_1 hybrid donor will later reject skin from one of the parent strains of the hybrid, and

have therefore presumably rejected the inducing cells which bear the same antigen, while at the same time showing a high degree of tolerance to grafts of skin from the other parent strain of the F_1 hybrid. Also, excision of a tolerated homograft in rats leaves behind a certain degree of tolerance to the re-establishment of further homografts from the original donor. A further interesting discovery is that grafts from male mice will not survive indefinitely on females of the same inbred line, although female isografts are fully acceptable to males.

The properdin system is described by R. J. WEDGWOOD (*The Properdin System and Immunity: a Review*, pp. 56–70), who points out that caution is needed in assuming that the properties of properdin which have been demonstrated *in vitro* necessarily apply also in the intact animal. The purely immunological section of the symposium is brought to an end with a contribution by V. A. NAJJAR and J. P. ROBINSON on *A Unified Concept in Immunological Reactions and Allergic States* (pp. 71–91).

In their paper *Studies on High Molecular Weight γ-Globulins and Their Complexes in Rheumatoid Arthritis* (pp. 92–99), E. C. FRANKLIN, G. EDELMAN and H. G. KUNKEL describe an unusual gamma globulin with a sedimentation constant of 22S which can be demonstrated in the sera of patients with rheumatoid arthritis, and which may amount to as much as 10–15% of the total serum proteins. This has been shown to be a complex consisting of approximately equal amounts of the normally-present 7S and 19S components, and it has also been demonstrated that it will react with antigen-antibody systems to form a precipitate. The topic of the purification of proteins is continued by J. R. CANN (*The Separation and Purification of Antibodies*, pp. 100–138) and D. H. CAMPBELL (*Some Problems in the Detection, Isolation and Purification of Antibodies*, pp. 139–143). The methods employed are described in detail, together with some of the difficulties which may arise. After a paper on *The Genesis of Fever in Infectious Disease* by W. B. WOOD, JR. (pp. 144–162), the last 96 pages of the symposium are devoted to virology.

SIR MACFARLANE BURNET begins with a historical review of the changing trends in research on bacteriophage (*From Bacteriophage to Influenza Virus*, pp. 163–175), in which he incidentally explains why the phenomenon of haemagglutination by influenza virus eluded the observation of experienced workers for so long. In *The Purification and Physicochemical Properties of Plant and Animal Viruses* (pp. 176–187) F. L. SCHAFFER describes the purification of poliomyelitis virus from brain homogenate and tissue culture fluid by precipitation at *p*H 4·5, elution at *p*H 9, extraction with butanol and high-speed centrifugation. S. E. LURIA, in *Viruses as Infective Genetic Materials* (pp. 188–195), gives a new definition of viruses, based mostly on work with phage, as "elements of genetic material that can determine, in the cells where they reproduce, the biosynthesis of a specific apparatus for their own introduction into other cells". The importance of phage in human medicine is discussed by N. B. GROMAN (*The Relation of Bacteriophage to Human Disease: a Review of Conversion to Toxigenicity in Corynebacterium diphtheriae*, pp. 196–205). Recent work has suggested that diphtheria toxin is liberated as the result of lysis of the bacterial cell produced either by the induction of a lysogenic strain or by the infection of a non-toxigenic strain by the converting phage. After a paper on plant viruses by H. FRAENKEL-CONRAT (*Tobacco Mosaic, a Molecular Infection*, pp. 206–210), the symposium ends with three instructive papers on poliomyelitis (*Characteristics of Naturally Acquired Immunity in Poliomyelitis and of Immunity Induced by Killed- and Live-Virus Vaccine*, pp. 211–232, by A. B. SABIN; *Immunity in Poliomyelitis Infection: Observations in Experimental Epidemiology*, pp. 233–245, by J. R. PAUL, D. M. HORSTMANN and J. C. NIEDERMAN; *The Influence of Artificial Immunization against Poliomyelitis upon Virus Dissemination*, pp. 246–258, by J. P. FOX).

D. J. Bauer

SPEER, V. C., BROWN, H., QUINN, L. & CATRON, D. V. **The Cessation of Antibody Absorption in the Young Pig.** *J. Immunology.* 1959, Dec., v. 83, No. 6, 632–4, 1 fig.

"Eight litters of nine pigs each were employed to delineate the length of time after birth that the baby pig is capable of absorbing antibodies from orally ingested colostrum milk, containing *Escherichia coli* antibodies. A sensitized sheep red blood cell haemagglutination test was used to detect the presence of the antibodies contained in the serum. It was found that the baby pig efficiently absorbed the *E. coli* antibodies at a very young age. This efficiency declined rapidly, following the first order reaction rate law, with a half-life absorption efficiency of 3 hr. Antibody absorption declined to insignificant amounts in baby pigs beyond 24 hr. of age."

BECKER, E. L. & NEFF, J. C. **Antigen-Antibody Reactions in Agar. IV. Concerning the Measurement of Antibody Concentration.** *J. Immunology.* 1959, Dec., v. 83, No. 6, 571–81, 3 figs. [15 refs.]

CARLISLE, H. N. & SASLAW, S. **Properdin Levels in Splenectomized Persons.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 150–54.

"Properdin titers were definitely lower in 105 splenectomized persons than in 113 normal, healthy subjects. Within the splenectomized group, there was no correlation between properdin level and age of individual, age at splenectomy, and years post-splenectomy. Properdin titers were significantly lower in splenectomized females, but the sex difference was minimal in comparison to the difference between total splenectomized and control groups. Suggestive evidence is presented that low properdin levels in splenectomized persons are related in part to absence of spleen."

SÜSSDORF, D. H. **Quantitative Changes in the White and Red Pulp of the Spleen during Hemolysin Formation in X-Irradiated and Nonirradiated Rabbits.** *J. Infect. Dis.* 1959, Nov.–Dec., v. 105, No. 3, 238–52, 5 figs. [25 refs.]

Book Review

CAMPBELL, Irene R. & WIDNER, Evelyn M., with the assistance of Irene P. KUKAINIS. Annotated Bibliography. **The Occurrence and Biological Effects of Fluorine Compounds. Vol. I. The Inorganic Compounds. Book 1.** pp. iv + 507. 1958. **Book 2.** pp. 509–955. 1958 (Printed 1959). Cincinnati 19: The Kettering Laboratory, Dept. Preventive Med. & Indust. Health, College of Medicine, University of Cincinnati, Ohio. [$25.00.]

This is an excellent bibliography which comes from the Kettering Laboratory in the Department of Preventive Medicine and Industrial Health, College of Medicine, University of Cincinnati, Ohio. It is a systematic and up-to-date compilation of nearly 8,700 references and abstracts of publications on the inorganic compounds of fluorine and "every attempt has been made to abstract the articles as completely as possible, to reveal the scope of the investigations, the concentrations employed in animal or human experiments or those existing in actual exposure, the number of animals used in the experiments, or any other qualifying information that may contribute to an understanding of the subject".

The arrangement of the large mass of material presented many problems but it was decided to group the references into chapters of which there are 16 in the 2 books comprising Volume I. Book I contains chapters concerning reviews and general discussions of hazards to health; general distribution of fluorine in the environment; physiological and pharmacological effects; observations on warm-blooded animals; observations on man; occupational hazards and their prevention and problems associated with pollution of air and water. Book II has chapters on legal aspects; dental health and fluorine; uses in therapy; uses as pesticides, growth regulators and preservatives; uses in industry; other uses; removal of fluorine from air, food, minerals and water; methods of analyses and on chemical and physical properties.

Information on any subject is easily obtained—articles and their abstracts are given chronologically in each chapter, the numbered pages of which give also the number of every article on that page. There are cross references at the end of each chapter. In addition there are first-rate detailed indexes of authors and of subjects.

These abstracts "are not intended as a substitute for the original publication for the final appraisal of the various problems. The compilation is rather intended to be a record of published material to aid investigators in the phases of interest in the compounds of fluorine within its coverage".

The aim of recording "as completely as possible, the literature pertaining to the natural and artificial occurrence of fluorine compounds in the environment of man, and their effects on all living organisms" has been achieved most admirably.

The publication is in clear mimeographic form with loose binding which permits the removal of individual pages.

M. E. Delafield

It is with deep regret that we record the death on 16th March, 1960 of John Constable Broom, *O.B.E.*, M.D., who made many valuable contributions to this *Bulletin* during the past 18 years on leptospirosis and the leptospires.

It is with deep regret that we record the death on 4th April, 1960 of Air Marshal Sir James MacConnell Kilpatrick, *K.B.E.*, *C.B.*, LL.D., M.B., D.P.H., Dean of the London School of Hygiene and Tropical Medicine, who had been a member of the Honorary Managing Committee of the Bureau of Hygiene and Tropical Diseases since 1957.

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